Parasomnias are physiologic and behavioral phenomena, which occur exclusively during, or are augmented by, the sleeping state. Two major groups of parasomnias can be identified, depending upon whether the symptom is a primary phenomenon of sleep itself, or a physiologic phenomenon augmented by sleep.

**I. Primary sleep phenomena**

The key to the understanding of the primary sleep parasomnias is the concept that sleep and wakefulness are not invariably mutually exclusive states. There may be the simultaneous occurrence or rapid oscillation of NREM sleep and wakefulness in the form of sleep-drunkenness, automatic behavior or “micro-sleeps.”

These primary sleep phenomena can be divided into REM and NREM categories—both normal and abnormal.

**A. REM sleep phenomena-normal**

Dreams and dream anxiety attacks represent normal REM phenomena.

**B. REM sleep phenomena-abnormal**

The dissociation of the components of REM sleep may result in bizarre experiences and behaviors. These symptoms, when occurring in isolation, are occasionally misinterpreted as manifestations of psychiatric disease, either by the afflicted individual or the physician. These include cataplexy, sleep paralysis, hypnagogic/hypnopompic hallucinations, REM sleep behavior disorder, and waking hallucinations.

**C. NREM sleep phenomena-normal**

Sleep starts (hypnic jerks) are experienced by many normal individuals just at sleep onset, in the transition between wakefulness and sleep. These normal physiologic events usually involve a sudden jerk of all or part of the body, occasionally awakening the victim or bed-partner. They may be associated with impressive visual (flashes of light, fragmentary visual hallucinations), auditory (loud bangs, snapping noises) or somesthetic (pain, floating, something flowing through the body) experiences. The sensory phenomena may occur without the body jerk.

**D. NREM phenomena-abnormal**

The most impressive NREM sleep phenomena are the “disorders of arousal”, which tend to arise from slow-wave
sleep. These have features in common: there is frequently a positive family history, which suggests a genetic component; they tend to arise from slow wave sleep (stages 3 and 4 of NREM sleep)—therefore usually occurring in the first third of the sleep cycle (and rarely during naps); and they are common in childhood—usually decreasing in frequency with increasing age. These occur on a broad spectrum ranging from confusional arousals, sleepwalking, and sleep terrors.

Although it is commonly felt that persistence of these behaviors beyond childhood or their development in adulthood is an indication of significant psychopathology, this is not necessarily the case.

E. Miscellaneous primary sleep parasomnias

There remain a number of primary sleep phenomena which are poorly understood, and which do not respect sleep stages. These include bruxism, enuresis, rhythmic movement disorder, and somniloquy.

II. Secondary sleep phenomena

The secondary phenomena are those parasomnias representing either abnormal or excessive autonomic or physiologic events occurring preferentially during sleep. These can be approached by organ system.

A. Central nervous system parasomnias

Seizures may occur frequently or exclusively during sleep. Nocturnal seizures are frequently mis-diagnosed due to bizarre seizure-related behaviors and absence of scalp electrode evidence of EEG seizure activity.

The headaches of cluster headache, chronic paroxysmal hemicrania, and possibly migraines have been shown to be REM sleep related, explaining the common report of sleep-related headaches in these conditions.

B. Cardiopulmonary parasomnias

Uncommonly, cardiac arrhythmias, angina pectoris, or asthma, may occur predominantly during sleep. Sleep-related expiratory groaning is another example.

Gastrointestinal parasomnias

A number of gastrointestinal events may result in paroxysmal arousals during sleep, often mimicking disorders of other organ systems. These include gastroesophageal reflux and diffuse esophageal spasm.

Miscellaneous secondary parasomnias

Panic attacks and muscle cramps may occur predominantly during sleep.

Summary

The discovery of REM sleep with its tonic and phasic components and the ability to monitor multiple physiologic variables during both wakefulness and sleep have permitted the identification and classification of a wide variety of unusual sleep phenomena. Integral to the understanding of many of these is the concept that wakefulness, REM sleep and NREM sleep are not mutually exclusive states, and may occur simultaneously, oscillate rapidly, or appear in dissociated form to produce primary sleep parasomnias. These often bizarre and frightening experiences may occur in normal individuals without evidence of either a psychiatric disorder or a primary sleep disorder, such as narcolepsy. And although it is commonly thought that somniloquy, sleep-walking and sleep terrors, enuresis, bruxism and nocturnal head-banging are usually associated with significant psychopathology, confirmative data are lacking.

Primary sleep parasomnias can frequently be diagnosed by history alone. Unusual or difficult cases should be studied in a comprehensive, well-equipped and experienced sleep disorders center to rule out secondary sleep parasomnias.

The secondary sleep parasomnias usually require formal polysomnographic study with extensive physiologic monitoring, as the nature of the clinical problem is often not apparent by history or physical examination.

Most unusual sleep-related events can be explained by already documented primary or secondary sleep parasomnias, and the list of identified conditions will undoubtedly grow as more sleep-related symptoms are adequately studied. This is fertile ground for the close collaboration between sleep medicine clinicians and basic science sle
This talk will review first briefly the evidence for the neurochemical adenosine’s being an important mediator of the homeostatic sleep drive, for the sleepiness that follows prolonged wakefulness. Then we will discuss a rodent (rat) model of the consequences of sleep apnea that separates the effects of sleep interruption and intermittent hypoxia. We will primarily focus on the model for sleep interruption, generated by a 30 sec of a slowly moving treadmill following by 90 sec of no motion during which animals are permitted to sleep. However the short duration of sleep is not sufficient to permit deep delta sleep; this loss of deepest sleep is similar to that of humans with sleep apnea. We find that rodents with this treatment have increased propensity to sleep, as do humans with sleep apnea, and that, in our animal model, this propensity is mediated by increasing levels of basal forebrain adenosine. Behavioral tests show that animals under this sleep interruption regimen have decreased attention (rat sustained attention test), have decreased spatial learning (Morris Water Maze), have a decreased neurophysiologic substrate for learning (long-term potentiation in hippocampus), and show deficits on set shifting (extra-dimensional shift test, a rodent analog of the Wisconsin Card Sorting Test). These cognitive deficits are similar to those in humans with sleep apnea and suggest a major role of sleep interruption in producing these deficits.

Memory Consolidation during Human Sleep

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The hypothesis that the formation of memory is an essential function of sleep has been around for a long time, but has received compelling experimental evidence only recently. Studies in humans show that sleep enhances the formation of hippocampus-dependent declarative memories as well as procedural memories which do not depend on the hippocampal activity. While the former benefits particularly from SWS dominating the early part of nocturnal sleep, the latter benefits particularly from REM sleep prevailing during the late part of the night. Sleep-dependent memory formation in both memory systems involves an active reorganization of representations that at later retrieval is expressed as behavioral improvement or gain of knowledge, respectively. Recent studies have elucidated some of the neurophysiological conditions underlying this sleep-associated memory formation in the declarative memory system. Slow oscillatory EEG waves and spindle activity arising from thalamo-cortical circuitry are likely to critically contribute to this process in close association with a covert replay of recently acquired memory representations. In humans and rats, intense hippocampus-dependent learning leads to enhanced spindle activity during subsequent periods of SWS-rich sleep. In addition, slow oscillations during post-acquisition sleep appear to synchronize spindle activity with memory replays occurring in neocortical and hippocampal neuronal networks. Thus, in human post-learning sleep, enhanced spindle activity is associated with a learning-dependent increase in neocortical EEG coherence during the depolarizing up-phase of the slow oscillation. In rats, the slow oscillatory up-phase is associated with an increased occurrence of hippocampal sharp wave–ripple events, an index of memory replay in hippocampal networks. Finally, hippocampus-dependent declarative memory formation during SWS-rich sleep can be blocked by cholinergic agonists suppressing hippocampo-neocortical signal transfer. On the whole, the data speak for an active consolidation of declarative memories during sleep, based on a hippocampo-neocortical dialogue synchronized by slow oscillations.
the recent progress in genome sequencing projects have
given rise to the expectation that the molecular pathways
underlying sleep disorders and sleep regulation or even
function can now be more readily identified. Recent
studies in the dog, the mouse, and the fruit fly have begun
to reveal exciting new molecular pathways that regulate
sleep. This illustrates that only the continued use of
multiple animal models and genetic approaches will
ensure a rapid progress in the relatively new field of
sleep genetics. Sleep disorders are highly frequent in the
general population and have dramatic health, social, and
economic impacts. Their treatments remain largely
symptomatic owing to our ignorance of their molecular
pathophysiology. The genetic dissection of well-charac-
terized sleep disorders such as narcolepsy might improve
our ability for better treatments and also provide
fundamental insights into the underlying neurobiological
bases of normal sleep and wakefulness.
MS 03: Main Symposium III

MS 03.01
Treatment effect of CPAP on cerebral tissue oxygenation during sleep in patients with OSAHS

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Objectives: To investigate the CPAP treatment effect on cerebral tissue oxygenation during obstructive sleep apnea.

Methods: Cerebral tissue oxygenation reflected by tissue oxygenation index (TOI) (1) in eighteen severe OSAHS patients with a mean AHI of 68±24 was monitored using near-infrared spectroscopy (NIRS) (Niro300, Hamamatsu Japan). Full polysomnography (PSG) and pulse oximetry measuring oxygen saturation (SaO2) were conducted simultaneously. The TOI signal was fed into one of the PSG channels and was displayed on the screen at the same time with other PSG tracings. SaO2 measurements include oxygen desaturation ≥4% index (ODI4), the lowest SaO2 (LSaO2) and the mean SaO2 (MSaO2) during sleep. TOI was given by the ratio of OHb to OHb+HHb. Parameters indicating cerebral tissue desaturation include numbers of TOI decrease ≥4% per hour (TOI4), the lowest TOI (LTOI) and the mean TOI (MTOI) during sleep. SaO2 and TOI indexes were also monitored simultaneously during CPAP treatment in fourteen of the 18 patients.

Results: AHI, ODI4 and TOI correlated very well with each other (AHI vs ODI4 r=0.879; AHI vs TOI4 R=0.568; TOI4 vs ODI4 r=0.729; all p<0.05) in 18 OSAHS patients. However, linear regression did not reveal any relationship between LSaO2 and LTOI, MSaO2 and MTOI during sleep. With the improvement of sleep apnea during CPAP treatment, both SaO2 and TOI increased significantly (Table 1).

Conclusions: Monitoring for cerebral tissue saturation during obstructive sleep apnoea provides additional information to conventional pulse oxygen saturation, and CPAP treatment improve both peripheral and tissue oxygenation.

Reference

MS 03.02
The association between oxidative stress and neuropsychological deficits in obstructive sleep apnea patients

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Aims: To study the relationship between oxidative stress and neuropsychological deficits as well as their reversion after CPAP therapy in patients with obstructive sleep apnea (OSA).

Methods: Nineteen men, with OSA diagnosis (apneahypopnea index above 10), with (mean±SD) age: 39±7, body mass index (BMI): 29±4 Kg/m² were compared with 12 volunteers matched for gender, age (36±7) and BMI (25±3 Kg/m²). All of them had more than 11 years of schooling. The protocol, in the first evaluation and after CPAP treatment for six months, included: full night PSG, Epworth Sleepiness Scale, neuropsychological tests (Toulouse Pieron, Wescheler Memory Scale, Wisconsin Test, Rey-Osterreith Complex Figure) and blood sample analysis (Superoxid Dismutase-SOD, Catalase, Gluthathione Peroxidase, Homocystein, and Vitamins E and C).

Results: When compared with controls, the patients showed a reduction of vitamin E level (10.5±3.3 umoles/L versus 19.2±7 umoles/L, p<0.0001), SOD (8.7±3.1 mU/mgHg versus 14.6±2.3 mU/mgHg p<0.0001) and also showed a poor performance of attention tests (Toulouse Pieron Errors: 0.95±1.43 versus 0.09±0.3, p=0.04) and of memory tests (WAIS R: 3.94±0.91, p<0.01 and Rey Figure Retrieval: 21.7± versus 29.4 ± p<0.001). There was a positive correlation between vitamin E and WAIS R (r=0.56; p=0.05). The use of CPAP improved the vitamin E level (from 10.5 to 15 umoles/L, p=0.03), SOD level (from 9 to 15 lmU/mgHg, p<0.0001) and the neuropsychological tests (WAIS R from 3.9 to 5.6

Table 1
<table>
<thead>
<tr>
<th>Arterial oxygen</th>
<th>Tissue oxygen</th>
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<tr>
<td>SaO2 Baseline</td>
<td>TOI baseline</td>
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<tr>
<td>DL4</td>
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<td>LSaO2</td>
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<td>MSaO2</td>
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Pre- treatment 95.2±2.9 59.1±24.7 61.6±16 89.4±4.8 68.0±4.4 21.8±15.4 50.7±6.3 65.8±3.6
CPAP treatment 96.0±1.3 2.8±3.4 92±1.0 95.9±1.1 68.7±4.0 1.1±1.0 57.4±6.9 68.3±4.0
P 0.198 0.000 0.001 0.586 0.000 0.006 0.031
MS 03.03
An evaluation of pulse transit time useful in differentiating respiratory event for patients with sleep breathing disorder

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Aims: Variation of inspiratory effort in sleep disordered breathing induces the oscillation in blood pressure, which correspond to pulse transit time (PTT) inversely. This study evaluated the feasibility of PTT as a visual parameter for differentiating respiratory event in patients with sleep breathing disorder.

Methods: Sixteen patients complained of snoring and sleep apnea were booked in the study. Polysomnographic data of Zopiclone induced daytime sleep were analyzed, PTT and intra-esophageal pressure (Peso) were assessed for each respiratory event.

Results: With compassion to Peso, the total accuracy of PTT was 51.8% for 1266 events. The relatively high coincidence rate could be observed in obstructive events (57.1%), with crescendo Peso pattern (71.5%), in lateral position (82.2%). PTT oscillation could only partly reflect respiratory rhythm to some degree (56.5%). Absolute PTT value presented a poor relationship with respiratory effort.

Conclusions: PTT coincided well with crescendo Peso in lateral position for obstructive events. PTT swings could only partly fit respiratory wave to some degree. Absolute PTT value and its change could not reflect respiratory effort. Although PTT is a non-invasive and convenient way for assessing inspiratory effort, its sensitivity varies to different events, respiratory patterns, positions, different patients and other situations, which limit its feasibility. Further work is required.

Background: Few published studies have previously examined the epidemiology of restless legs syndrome (RLS) among African Americans, relative to other racial groups. Due to the relative absence of African-Americans seeking treatment for RLS in specialty clinics, a lower prevalence of RLS among African-Americans than whites has been suggested.

Objective: To compare the point-prevalence of restless legs syndrome and its associated risk factors in African Americans and whites in a biracial community sample.

Design: Household-based, cross-sectional assessment of RLS as part of Wave IV of the Baltimore Health and Mental Health Study. Subjects: Subjects included 982 adults (344 African Americans, 607 whites, and 31 others) in Baltimore, Maryland.

Main Outcome Variable: Diagnosis of RLS based on endorsement of RLS symptoms by participants who responded to a RLS Questionnaire during a household interview.

Results: The point prevalence of RLS in this population was 4.1%. The rates were similar for African Americans (4.5%) and whites (3.9%). After adjustment for age, gender, medical co morbidities, and socioeconomic status, no difference in the point-prevalence of RLS was found between African-Americans and whites.

Conclusions: RLS is comparably prevalent in African-Americans and whites. Barriers affecting access to care settings for African-American RLS patients should be investigated in the future.

MS 03.04
Lack of Racial Disparity in the Prevalence of Restless Legs Syndrome in a Biracial East Baltimore Population: Preliminary Findings from the Baltimore Health and Mental Health Study

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Methods: Thirty healthy adults (mean age 31.3±11.5) and 27 EDS patients (47.0±13.7) with valid driver’s licenses were included; normative subjects were screened for significant medical, psychiatric or sleep disorders, and use of psychotropic medications. EDS patients qualified by reporting an Epworth Sleepiness score >10 or recent...
afternoon in this group. With an increasing trend towards crash-proneness in the late afternoon drives, with this circadian effect appearing most significant diurnally. Tracking did not differ between groups, although some subjective ratings, RT, crashes and MS. Mean values of each variable were attained and analyzed using a general linear model and independent t-tests.

Results: In comparing normative individuals and EDS patients, significant differences were found between subjective ratings, RT, crashes and MS. Mean speed and tracking did not differ between groups, although some diurnal variation was noted for speed. Both groups showed a significant diurnal trend of relative RT slowing during afternoon drives, with this circadian effect appearing most pronounced for EDS patients. Objective EEG MS monitoring demonstrated escalating sleep intrusion with repeated drives in both groups, but particularly for the EDS group. Total crash rates were three times higher in EDS patients, with an increasing trend towards crash-proneness in the late afternoon in this group.

Conclusions: We have demonstrated significantly impaired performance on some, though not all, driving parameters. The presence of circadian variation in performance appears to suggest a role for multiple driving tests. While increased crash rate is the most dramatic of these, slowing of RT was most significant. EEG monitoring was able to document increased propensity towards MS episodes in patients with EDS, which we suggest is causative in creating this impairment. It remains unclear whether a neurophysiologic or simulator approach captures impairment due to sleepiness with greater sensitivity and specificity. A hybrid approach combining data from both sources seems optimal, and also could be integrated in commercial vehicle use.

MS 03.06 Olfactory Impairment in Idiopathic REM Sleep Behavior Disorder

Fantini ML, Postuma R, Montplaisir J, Ferini-Strambi L

Aims: REM sleep behavior disorder (RBD) is a parasomnia characterized by vigorous motor activity during REM sleep. Idiopathic RBD (iRBD) often heralds an alpha-synucleinopathy, including Parkinson’s disease (PD), dementia with Lewy bodies (DLB) and multiple system atrophy. Olfactory impairment is a frequent early feature of PD and DLB, often preceding by several years the motor and/or cognitive symptoms. If idiopathic RBD is an harbinger of a Lewy body disease, olfactory deficit would be expected in these patients. The aim of the study was to assess olfactory function in idiopathic RBD, compared to control subjects.

Methods: Fifty idiopathic polysomnographic (PSG)-confirmed RBD patients (41M:9F; mean age: 69.1 ± 9.0 yrs.) and 50 gender and age-matched healthy control subjects (41M:9F; mean age: 69.9 ± 9.0 yrs.) were studied. Subjects underwent the Brief Smell Identification Test (B-SIT), a smaller and cross-cultural 12-items version of the University of Pennsylvania Smell Identification test (UPSIT), and a standard neurological examination including the motor scale of the UPDRS. All participants were free of psychotropic medications that may influence dopamine system and olfactory function and none had an history of nasal surgery (except septoplasty), head trauma, pulmonary disease, endocrine disorders, perennial allergies, drug or alcohol abuse.

Results: Mean B-SIT score was significantly lower in patients with iRBD (7.0 ± 2.5, range: 2–11) compared to control subjects (9.4 ± 1.8, range: 6–12; p < 0.0001). RBD patients showed a greater heterogeneity in odour identification scores than controls. In RBD patients no correlation was found between B-SIT score and either RBD duration, frequency or UPDRS score.

Conclusions: The present study showed an olfactory impairment in iRBD. Hyposmia in iRBD may represent a sign of an impending neurodegenerative process, particularly a Lewy bodies disease. Assessment of olfactory function in this population may help to identify subjects at higher risk for developing a neurodegenerative disease.

MS 03.07 Screening and treatment of obstructive sleep apnea hypopnea syndrome in severely disabled patients-a clinical challenge

Nishimura K, Ohba S, Tachibana N, Taniike M

Aims: REM sleep behavior disorder (RBD) is a parasomnia characterized by vigorous motor activity during REM sleep. Idiopathic RBD (iRBD) often heralds an alpha-synucleinopathy, including Parkinson’s disease (PD), dementia with Lewy bodies (DLB) and multiple system atrophy. Olfactory impairment is a frequent early feature of PD and DLB, often preceding by several years the motor and/or cognitive symptoms. If idiopathic RBD is an harbinger of a Lewy body disease, olfactory deficit would be expected in these patients. The aim of the study was to assess olfactory function in idiopathic RBD, compared to control subjects.

Methods: Fifty idiopathic polysomnographic (PSG)-confirmed RBD patients (41M:9F; mean age: 69.1 ± 9.0 yrs.) and 50 gender and age-matched healthy control subjects (41M:9F; mean age: 69.9 ± 9.0 yrs.) were studied. Subjects underwent the Brief Smell Identification Test (B-SIT), a smaller and cross-cultural 12-items version of the University of Pennsylvania Smell Identification test (UPSIT), and a standard neurological examination including the motor scale of the UPDRS. All participants were free of psychotropic medications that may influence dopamine system and olfactory function and none had an history of nasal surgery (except septoplasty), head trauma, pulmonary disease, endocrine disorders, perennial allergies, drug or alcohol abuse.

Results: Mean B-SIT score was significantly lower in patients with iRBD (7.0 ± 2.5, range: 2–11) compared to control subjects (9.4 ± 1.8, range: 6–12; p < 0.0001). RBD patients showed a greater heterogeneity in odour identification scores than controls. In RBD patients no correlation was found between B-SIT score and either RBD duration, frequency or UPDRS score.

Conclusions: The present study showed an olfactory impairment in iRBD. Hyposmia in iRBD may represent a sign of an impending neurodegenerative process, particularly a Lewy bodies disease. Assessment of olfactory function in this population may help to identify subjects at higher risk for developing a neurodegenerative disease.

Patients with severe physical and mental disabilities who are institutionalized often with unestablished diagnosis are at high risk for sleep disordered breathing (SDB) because these patients often have facial dysmorphism, severe somatic deformity, and abnormal muscle tone. Moreover, the concomitant SDB may make their quality of life worse. However, it is technically and economically difficult to investigate their sleep and respiratory abnormality by using conventional polysomnography (PSG), and there have not
been enough studies about this group of patients. We utilized pulse oxymetry (PO) for screening OSAHS in institutionalized patients with severe physical and mental disabilities and treated severe cases with nasal CPAP (nCPAP) and chin equipment. We performed nocturnal PO using Wrist SO2 (Koike Medical, Tokyo, Japan) for screening OSAHS in 14 severely handicapped people (7M/7F, 35.2 ± 7.6 years of age, range 25–53) who were suspected to have OSAHS by the inclusion criteria of habitual snoring and frequently witnessed apnea out of 177 inmates at Sunago Institute. We used the number of events in which oxygen desaturation fell by ≥ 3% per hour (3% oxygen desaturation index, 3%ODI) as the indicator of OSAHS. The percentage of the recording time in which SpO2 showed less than 90% to the total recording time (%Time SpO2<90%) was used for another indicator to present the severity of hypoxia during sleep. Three showed 3%ODI ≥ 30/h (severe), and in 2 (Patients A & B) out of these 3 cases, %Time SpO2<90% was over 10% and mean SpO2 was below 95%. 3%ODI was 10–30 in 9 (moderate) and 5–10 in 1 (mild). Overnight PSG was undergone with Ps A & B, revealing that AHI were 229.2 and 62.6 respectively. Although the patients were uncooperative and wear a mask, nCPAP (Goodknight 418P:Puritan Bennett) was initiated with desensitization process for several months. Optimal pressure was determined by the raw data of nocturnal PO. The repeated PO with nCPAP showed clear improvement in Ps A & B (3%ODI:63.7 to 2.2, 36.2 to 6.1; %Time SpO2<90%:76.0 to 0, 19.5 to 0). Clinically both Ps A & B were more alert in the daytime, and they showed more regular sleep/wake cycles after treatment. In one moderate case (Patient C), hand-made equipment to lift up the lower jaw (Kawamura-Gishi, Osaka, Japan) improved nocturnal desaturation (%ODI:27.8 to 15.6, %Time SpO2<90%:5.9 to 4.2). The other 11 patients were kept in an optimal sleep position to prevent airway obstruction. We concluded that severely disabled patients had a high risk for OSAHS, and that screening OSAHS by nocturnal PO is useful and workable for these patients. In most severe cases nCPAP treatment was confirmed to be effective to improve their quality of life. More systematic study for determining the optimal treatment options for less severe OSAHS cases in this group of patients are required.

Background: Chronic sleep onset insomnia (SOI) in Attention-Deficit/Hyperkinesia Disorder (ADHD) is usually attributed to pedagogical insufficiency of the parents or to the ADHD disorder itself. Some preliminary studies suggested that the biological clock might be disturbed in ADHD. To know if sleep hygiene in ADHD children with chronic insomnia differs from that in ADHD children with normal sleep and to assess the biological clock in these children we performed several studies.

Methods: Medication naïve children, aged 6–12 yrs, with rigorously diagnosed ADHD and healthy controls were studied. Sleep hygiene was measured using the internationally validated Children’s Sleep Hygiene Scale (CSHS). Sleep was assessed actigraphically. The biological clock was assessed by measuring Salivary Dim Light Melatonin Onset (DLMO). Per3 clock gene was measured using sweep swap samples.

Results: Mean [SD] CSHS scores of 74 ADHD children with SOI (56.4 [10.5]) did not differ (p=0.17) from those of 23 ADHD controls without SOI (53.0 [10.6]). Sleep onset in 87 ADHD-SOI children (21:38 [0:54] h.) was significant later than in 33 ADHD children without SOI (20:55 [0:37] h.) DLMO in the ADHD-SOI children (20:32 [0:55] h.). The 4-and 5-repeat alleles of Per3 clock gene of 10 ADHD children with severe SOI and very late DLMO did not differ from those of 10 healthy controls. Details are reported in several posters presented at the congress

Conclusions: Sleep onset insomnia in ADHD children with chronic sleep onset insomnia is not caused by insufficient sleep hygiene. Probably a biological clock disturbance, characterized by a delayed melatonin onset is the major etiological factor. The Per3 clock seems to be normal.

MS 03.08

‘Idiopathic’ chronic sleep onset insomnia in ADHD children is caused by a circadian rhythm disorder

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MS 03.09

Sleep Complaints, Cardiovascular Pathology and Quality of Life of the Population of West part of Lithuania

Varoneckas G, Andruksiene J, Staniute M, Martinkenas A

Institute of Psychophysiology and Rehabilitation c/o Kaunas University of Medicine

Aim: was to assess the association between sleep complaints, cardiovascular pathology and health-related quality of life among the citizens of West part of Lithuania.

Methods: Randomly selected 1602 citizens, aged 35–74 years, of Palanga city located in West part of Lithuania were investigated. All persons have filled Basic Nordic Sleep Questionnaire and were screened by ECG and Rose angina questionnaire, 1015 of them have filled SF-36 additionally. All respondents according to sleep complaints and their frequency evaluated by Basic Nordic Sleep Questionnaire (SSRS, 1988) were divided into good (248 subjects) and poor (1348 subjects) sleepers’ groups. The SF-36 was used to assess the health-related quality of life. It included one multi-item scale that assessed eight health domains:
physical functioning (PF), physical role limitations (RP), emotional role limitations (RE), social functioning (SF), mental health (MH), energy/vitality (EV), bodily pain (P) and general health perception (GHP). Coronary artery disease (CAD) diagnosis was based on typical electrocardiographic findings and symptoms reported by the respondents (Rose angina questionnaire). Arterial hypertension was diagnosed according to WHO criteria (1999), mean score of three times measured blood pressure ≥140/90 mmHg. The statistical analysis of the data was performed using program STATISTICA.

Results: Even 85% of respondents were proved as poor sleepers. They had complaints of difficulty falling asleep, frequent awakenings, early morning awakenings. Hypertension was more prevalent among poor sleepers, as compared with good ones (respectively, 9.0% and 7.3%, p > 0.05). In 1048 subjects the cardiovascular pathology was not found. Arterial hypertension was observed in 139 subjects, CAD-in 232 subjects and both, arterial hypertension and CAD-in 183 subjects. Among poor sleepers, as compared with good sleepers, arterial hypertension (9.0% and 7.3%, p > 0.05, respectively) and CAD (15.1% and 11.3%, p > 0.05, respectively) was more prevalent. There was no statistically significant difference in prevalence of both pathologies, arterial hypertension and CAD, in good (12.1%) and poor (11.4%) sleepers. Poor sleepers were characterized by statistically significant worse health related quality of life in all domains (PF: 83.1% vs. 73.5%, RP: 74.8% vs. 62.4%, RE: 77.2% vs. 63.7%, SF: 85.0% vs. 71.7%, MH: 73.1% vs. 63.2%, EV: 68.3% vs. 58.2%, P: 76.8% vs. 65.1%, GHP: 56.5% vs. 47.6%, respectively in good and poor sleepers).

Conclusions: Poor sleep was associated with more frequent prevalence of cardiovascular pathology (coronary artery disease and arterial hypertension) and reduced health related quality of life.

MS 03.10
Gender differences in old age regarding overnight procedural memory consolidation and the function of REM sleep

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Aims: Memory consolidation during sleep has mainly been studied in younger adults in the past. Recent findings suggest that the memory enhancing effects of REM sleep with regard to procedural memory consolidation may be less pronounced in older adults. Moreover, gender differences in several parameters of sleep have been reported for older adults. Based on these findings, the present study investigated if gender has an impact on overnight procedural memory consolidation in old age and whether REM sleep plays a role in this context.

Methods: Evening and overnight skill acquisition was investigated in 107 healthy older adults (mean age ± SD: 66.1±5.1; 51.4% female). Participants had been randomly assigned to five experimental groups of REM sleep manipulation based on deprivation and augmentation paradigms. Before and after the study night, procedural memory performance was tested in a mirror tracing task, consisting of seven practice pictures in the evening and one in the morning as well as six more complex test pictures performed in the evening as well as in the morning. Gender effects regarding evening and overnight skill acquisition were investigated in the practice and test pictures, while statistically controlling for group effects.

Results: REM sleep duration in minutes differed significantly between the five experimental groups during the study night [F (4, 102) =57.835, p < .001], which indicates that REM sleep duration had been successfully manipulated. No gender difference was observed for evening skill acquisition in the practice pictures [F (6, 77) = .509, ns], whereas a significant gender effect was found when morning performance in the practice picture was included in the analysis [F (7, 76) = 3.058, p < .01], with women showing higher overnight improvement rates than men. In line with this finding, gender also had a significant impact on overnight improvement in the test pictures [F (1, 86) = 14.194, p < .001]. Notably, a significant interaction between gender and REM sleep duration was found in this context [F (1, 84) = 4.134, p < .05], suggesting that women benefited more from REM sleep with regard to procedural memory consolidation than men.

Conclusions: Older women show higher benefits from REM sleep with regard to skill acquisition than men, possibly due to gender-related differences in REM sleep characteristics of old age.

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TS 01: Towards professional Sleep Medicine - Approaches in different parts of the world

TS 01.01
History of the Development of Sleep Medicine in the United States

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Major advances in chronobiology, basic and clinical sleep science over the past 50 years have led to the development of a sufficient body of information that has provided a scientific basis for Sleep Medicine to evolve as an independent area of specialty medical practice. This progress along with patient demand and increasing recognition that disorders of sleep are highly prevalent in the US population has led physicians to acquire the knowledge necessary for the diagnosis and treatment of disorders of sleep. This symposium presentation will review the development of the major professional organizations devoted to further the development of sleep science and medicine in the United States. It will include discussion of the American Academy of Sleep Medicine, the Sleep Research Society, Board certification of professionals, accreditation of Sleep Centers and Sleep Fellowship educational programs. The strategic initiatives taken by the professional organizations will be emphasized as a roadmap to assist other societies striving to achieve recognition of Sleep Medicine as an independent area of medical practice in their own country.

TS 01.02
Towards accreditation of Sleep Medicine in different European countries

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Sleep Medicine is a relatively young medical specialty that has its roots in both basic sleep research and specialized medicine. Being a ‘horizontal’ specialism, sleep medicine cuts across different ‘vertical’ specialties, such as neurology, psychiatry, pneumology, etc. In this respect sleep medicine shares common features with other specialties, such as oncology, infectiology, etc., disciplines that are not confined to one organ system. Because of this very nature, the process of giving credit to the new specialty may be problematic. Peer organizations representing the ‘vertical’ specialties may oppose this process, as the accreditation of the new may adversely affect in part the authority of the established disciplines. Accreditation of sleep medicine may therefore prove to be a time-consuming, laborious process that requires the ongoing effort of many professionals, wanting to reach the ultimate goal: obtaining an independent accreditation status from the Health Authorities of their country. While this accreditation process is now firmly established in the USA, Germany is the one and only country in Europe that has reached a similar status. Other European countries, e.g. France and Italy, have accreditation facilities at the level of the National Sleep Societies. Substantial efforts should be made to introduce the concept of accreditation in other European countries and to promote the accreditation status from the level of the National Sleep Society to the specific National Health system in the different countries.

TS 01.03
Accreditation of Sleep Laboratories in South America

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TS 01.04
Development of Sleep Medicine in China

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TS 01.05
How Somnology became an accredited specialty in Germany

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The title sounds like a historical fairytale. But the dreams of the members of the German Sleep Society (DGSM) became reality in 2004 by the accreditation of Sleep Medicine by the German Chamber of Physicians. After passing in all federal countries at the end of 2005 “Sleep Medicine” will be a subspecialty in Pneumology,
Neurology, Psychiatry, Pediatrics, ENT-Medicine and Psychotherapy all over the country.

Since its foundation in 1992 the German Sleep Society with about 2020 members developed a network of "Sleep Medicine" in Germany. Besides quality assurance with accreditation of Sleep Medicine Centers (n=320) and performing process quality assurance by a peer review procedure and outcome measurements the qualification of physicians, scientists and technicians was one of the main tasks the DGSM wanted to work at.

After founding an interdisciplinary committee for the "Qualification Certificate of Somnology" in 1997 by the DGSM the duration of fulltime job training (18 months) and the main points of practical and theoretical knowledge in Sleep Medicine had to be defined. Additionally the Society organized an interdisciplinary curriculum of 200 hours concerning theory and practice in Sleep Medicine. The participation in this curriculum was voluntary, but it was recommended to take part because at the end of the training there was an examination in theory and practice of Sleep Medicine. Nowadays about 500 members of the DGSM had passed this examination and are so-called "Somnologists of the DGSM".

Essential for the one to one copy of this procedure from the unofficial title of DGSM – Somnologist to the official accreditation of the subspecialty of “Sleep Medicine” was that from the beginning in our society we tried to do the same procedures as they would have been done in the official procedure of the Chamber of Physicians. Among the federal countries Bavaria has been the fastest and there we got the first two official "Sleep Medicine" physicians in Germany. They did not fall from Heaven as it would have been in a fairytale, but they examined each other and thus the subspecialty was born.

**TS 02: The iron-dopamine connection in the Restless Legs Syndrome: Brain iron insufficiency producing hyper-dopaminergic state for RLS**

**TS 02.01**

**Oral and IV iron treatment of RLS: implications for iron metabolism**

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Nordlander in 1953 noted that his patients with RLS had a high prevalence of iron deficiency and that their symptoms improved upon treatment of the iron deficiency. More recently studies using CSF, MRI and autopsy material have supported the role of low brain iron in RLS. Since iron deficiency appears to play a central role in RLS, then iron treatment would be the next logical step. Most of the studies that have reported a benefit of oral iron treatment in RLS have been open-label design and had been in patients with low or deficient iron stores. There is one randomized, double-blind study of oral iron therapy in RLS, which showed no benefits, but also showed no change in body iron stores with treatment. Nordlander successively treated 21 out 22 RLS patients with intravenous iron. Earley etal found 6 out of 10 RLS subjects had complete resolution of symptoms and improvements in the PLM rates, following a single 1000 mg iron infusion. Despite the initial improvements, the majority of patients in both studies had a return of symptoms by 5–6 months. Further supplemental infusions of iron were effective in treating some subjects whose symptoms returned. However, the most significant finding was the rate of decline in serum ferritin following the infusions, which suggests that patients were losing iron at a rate 2–11 times greater than predicted. The iron loss explains the limited benefits of large iron infusions and the need for supplemental treatments. However, the metabolic bases for the iron loss is unclear. Despite the potential value of iron treatment for RLS, we still do not know the long-term consequences that maintaining high iron levels will have on various tissues in the body.

**TS 02.02**

**Relation of brain iron deficiency measures to clinical status of RLS**

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Both MRI and CSF measures show decreased brain iron for RLS patients compared to controls that appears specifically significant for the substantia nigra (SN) that was greater for morning than night time CSF tests. An evaluation of the clinical status of the patients shows a relation between CSF iron measures and age-of-onset of RLS suggesting this assessment reflects the status of a persisting underlying pathology whose severity indicates vulnerability to RLS and affects age at which RLS symptoms start occurring. The SN MRI in contrast related to current symptom severity reflecting current brain iron status in an area both apparently particularly sensitive to iron loss and critical for the dopaminergic system. Analyses comparing RLS and control dopamine (DA) and serotonin (5HT) related proteins from morning and night samples show no significant differences except for dramatically larger amounts of 3-oxymethyldopa (3-OMD) in both night and morning evaluations and an increased tetrahydrobiopterin (BH4) in the morning but not night samples. Combining the dopamine and iron CSF findings with the clinical symptoms indicates RLS patients support a putative increased amplitude of circadian pattern of iron demand and dopamine production. In the proposed model the dopamine production increases more in the early morning leaving a
relative deficits in the evening and night consistent with the circadian pattern of RLS symptoms and in particular the ‘protected period’ in the morning when RLS symptoms are the least severe if present at all. The data also suggest the brain iron deficiency overall produces a hyper-dopaminergic state with dopamine production increased compared to normal status.

**TS 02.03**  
**RLS animal models and cell culture: interactions between cellular iron deficiency and CNS dopamine**

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**Aims:** The direct relationship between brain iron content and dopamine biology is still under question and the role of the iron-dopamine relationship to RLS etiology is examined in rodent and cell culture models.

**Methods:** Both recombinant inbred strains of mice and Sprague Dawley rats have been used to examine the biology of iron and dopamine in rodents. Dietary treatments where iron content is varied between very low (<2 µgFe/mg diet) and very high (>350 µg Fe/mg). Dopamine biology is explored using in vivo microdialysis, HPLC-EC, radioligand binding of brain slices with autoradiography while cell culture approaches in PC12 cells and neuroblastoma cells also utilize iron chelation and iron loading to examine monoamine-cellular Fe inter-relationships.

**Results:** Dietary iron deficiency results in lower brain iron content, elevated striatal extracellular dopamine, decreased dopamine and norepinephrine transport, decreased dopamine D2 receptor densities, and elevations in activated tyrosine hydroxylase. In vitro culture studies reveal altered membrane trafficking of the dopamine transporter and increased rates of degradation when cells are treated with an iron chelator, desferroxamine.

**Conclusions:** Studies in rats and mice show both genetic and dietary factors can lead to alterations in brain iron content with resulting changes in dopamine metabolism.

**TS 02.04**  
**Autopsy evaluation of iron and dopamine status in RLS brains**

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**Aims:** To determine the profile of iron management proteins and dopamine in the nigrostriatal pathway in Restless Legs Syndrome.

**Methods:** Brains were collected at autopsy from individuals with primary RLS. Homogenates of the putamen and substantia nigra were collected and the expression pattern of iron management proteins and components of the dopaminergic system (e.g. dopamine, D2/D3 receptors, DAT, tyrosine hydroxylase) were quantified. In addition, neuromelanin cells were isolated by laser capture microdissection and subjected to the same analyses.

**Results:** The iron management proteins in these brain regions and in the neuromelanin cells indicate that there is an insufficient amount of iron available. There is one exception to this latter statement which is the expression of transferrin receptors. When iron levels are insufficient, transferrin receptor expression is elevated. However, in the RLS brain and cell homogenates, transferrin receptors are decreased. There is also a decrease in the iron regulatory protein (IRP1) that is responsible for stabilizing the mRNA for the transferrin receptor. Dopamine and neurtensin expression were significantly elevated in the substantia nigra and putamen in individuals of RLS. The concentration of Tyrosine Hydroxylase (TH) and phosphorylated TH was also increased in these brain regions in RLS compared to controls. There were no significant changes in the expression of DA receptors 2/3 or the DA transporter. Dopamine and neurtensin expression and the concentration of TH and phosphorylated TH were increased in the isolated neuromelanin neurons from RLS brains.

**Conclusions:** There is insufficient iron status in the nigrostriatal pathway in RLS brains that may be attributable to a decrease in expression of an iron regulatory protein whose function is to stabilize transferrin receptor mRNA. The elevated levels of phosphorylated TH suggest that there are adequate levels of activated TH in RLS. This finding is consistent with the elevated levels of dopamine. RLS patients frequently respond to treatment with low levels of dopamine agonists. Therefore our autopsy data and the clinical data suggest that the underlying problem in RLS is not a dopamine deficiency but a decrease in the integrity of the dopaminergic synapses.

**TS 03: Transport Noise and Sleep**

**TS 03.01**  
**Aircraft Noise Effects on Sleep: Results of 2240 Polysomnographically Recorded Subject Nights in Laboratory and Field Studies**

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**Aims:** Sleep is vital for the recovery of physical and mental capacities. Environmental noise potentially disrupts the sleep process and may lead to an extrinsic sleep disorder. In order to develop scientifically sound criteria for the
restriction of nocturnal air traffic, the DLR-Institute of Aerospace Medicine investigated the influence of nocturnal aircraft noise on sleep, mood and performance in four laboratory and two field studies between 1999 and 2004.

Methods: In the laboratory, 128 subjects aged 18–65 (53 male) were investigated during 13 consecutive nights (total: 1664 nights). Between 4 and 128 aircraft noise events (ANEs) with maximum sound pressure levels (SPLs) between 45 and 80 dB(A) were played back between 11 p.m. and 7 a.m. during nights 3 to 11. Results were compared to the findings of two field studies conducted at Cologne airport with 64 subjects (aged 19–61, 29 male) and 576 nights in total. Here, SPLs were simultaneously measured indoors and outdoors. Electrophysiological signals included polysonomography, EKG, plethysmography, respiration and actigraphy. Synchronous recording with acoustic data assured event related analysis. Mixed models and random effects logistic regression were used for analysis of changes in sleep structure and for calculation of dose-response curves.

Results: In the laboratory and based on TIB, aircraft noise was associated with signs of sleep fragmentation, as both amounts of Stage 1 (p < .001) and the number of awakenings (p < .001) were significantly increased. Additionally, SWS was significantly reduced by 5.1 min (p < .001) in exposure compared to baseline nights. Unexpectedly, total sleep time increased on average by 2.5 min (p = .354), most probably caused by a statistically significant reduction in sleep onset latency (p = .002) and decrements in the duration of spontaneous awakenings in exposure nights. Both may be interpreted as adaptation mechanisms to minor partial sleep deprivation of previous exposure nights. Fractions of Stage 2 (p = .110) and REM (p = .319) were non-significantly increased. Dose-response relationships with both increasing number and maximum SPL of ANEs were observed as well as a prominent first-exposure-night effect. In the field, aircraft noise lead to no obvious changes in sleep structure. Additionally, at the same maximum SPL awakening probability was much lower in the field compared to the laboratory. Based on these results, new criteria for the restriction of nocturnal air traffic were developed and will be exemplified for the extension of the airport Leipzig/Halle.

Conclusions: Altogether, 2240 subject nights were recorded with identical methodology in the laboratory and in the field. This large database and new statistical procedures allow for a precise prediction of the influence of nocturnal aircraft noise on sleep, which again can be used as guidelines for proposing enhanced laws for the protection of residents living near airports.

TS 03.02
Effects of Nocturnal Aircraft Noise on Performance, Annoyance and Stress Hormone Excretion-Overview and Results of the DLR-Study

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Aims: From 1999 to 2004, the DLR-Institute of Aerospace Medicine studied human reactions to nocturnal aircraft noise in laboratory and field experiments in order to develop statistically sound criteria for the protection of residents living in the vicinity of airports.

Methods: In total, 192 healthy volunteers (m/f), aged between 18 and 65 years, underwent altogether 2240 study nights. In the isolation facility of the institute, 128 subjects were examined during 13 consecutive nights. 16 subjects served as control. For 112 subjects, aircraft noise events were applied between 4 and 128 times per night with maximum sound pressure levels (SPLs) between 45 and 80 dB(A). Sleep disturbances were assessed by EEG, EOG, EMG and EKG, by respiration, finger-pulse amplitude and position in bed. These signals were simultaneously recorded with the acoustic signals for calculating event-correlated reactions. The concentration of cortisol, epinephrine and norepinephrine was determined from all night urine samples. At evening and morning, performance tests and questionnaires (fatigue, well-being, annoyance) were applied. These data and results were validated in two field studies with 64 volunteers during 9 consecutive nights at their homes near Cologne airport.

Results: Performance and most of the psychological parameters did not show significant dose-effect relationships, whereas annoyance on night aircraft noise did. Epinephrine and norepinephrine did not alter under nocturnal aircraft noise, cortisol excretion only changed under laboratory conditions. When effects occurred, they were much less pronounced in the field than in the laboratory.

Conclusions: The results of these studies contribute profound experimental knowledge to the very controversial disputes about the degree of impairing effects on human specific reactions to nocturnal aircraft noise.

TS 03.03
Aircraft noise and sleep disturbance: dose-response relationships and habituation issues

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Aims: The relationship between the level of aircraft noise events (ANE) and the extent of cortical and autonomic arousal during sleep was studied in a field-experiment. Dose-response relationships and the rate of habituation for individuals in their own homes, which were not habitually subjected to aircraft noise, were studied.

Methods: Twenty-one paid subjects (11 men) aged 22–37 were recorded (EEG, EOG, EMG, ECG) by conventional
methods, at home, in a community that is not habitually subjected to environmental noise, for three consecutive nights in which normal habits were retained. 16 pre-recorded aircraft noises were presented quasi-randomly each night. The ANE were delivered at 4 peak noise levels (50, 55, 60 and 65 LaMax dBA), so that 4 ANE at each level were presented in random order each night. The polysonmographic data was scored visually and analyzed blind for sleep stages and arousals, together with computer based analysis of heart rate responses (HRR). Inherent and evoked arousals were investigated in response to noise level, sleep stage, night number, time of night and subject age and gender.

Results: Autonomic responses (HRR-heart rate responses) to ANE were twice as likely to occur (84%) compared with both background & control arousals (42%). However, there was little variation in HRR rates for the different noise levels (ie. no dose-response). In comparison, the cortical arousals were five times more likely to be evoked than background or control arousals (62% of ANE compared with 12% for no-noise condition) and there was clear progressive disturbance as the noise level increased (dose-response) for the more major types of cortical arousal. There was evidence of habituation with moderate but significant progressive reduction across the three nights in mean subject response rates, particularly for major EEG responses including shifts to wake. However, autonomic arousals (HRR) showed no evidence of habituation.

Conclusion: Aircraft noise caused both cortical and autonomic arousals but the cortical responses were more specific and displayed clear dose-response relationships to noise levels. Autonomic arousals were more sensitive but less specific for aircraft noise. Habituation to aircraft noise was evident in the cortical (EEG) responses but not with the autonomic (HRR) responses.

TS 03.04
The significance of traffic mode on the extent of noise-induced sleep disturbances. Comparison between noises emitted from road, rail and air traffic

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Aims: Concerning transportation noise, aircraft noise annoys most and railway noise the least where road traffic noise has an intermediate position. As the information content is decisive for the effects of noise on sleep the same rank order was assumed for sleep disturbances as caused by noises emitted from these three traffic modes and the same was expected for the after-effects, namely subjective sleep quality and performance.

Methods: Sixteen women and sixteen men (19–28 years) slept, after a habituation night 4 nights each during 3 consecutive weeks in the laboratory from 2300 to 0700 hours. Eight persons slept in quiet throughout (pink noise, 32 dBA). Twenty-four persons were exposed with weekly changes to road-, rail-, or aircraft noise, respectively. Each week consisted of a random sequence of a quiet night (pink noise, 32 dBA) and 3 nights with equivalent noise levels of 39, 44, and 50 dBA indoors and maximum levels ranging from 50 to 62, 56 to 68, and 62 to 74 dBA indoors, respectively. The polysomnogram (2 EEG, 2 EOG and the electrocardiogram (ECG) was recorded throughout all nights, sleep quality was assessed and performance tests focussed on executive functions (shifting, updating, inhibition) were completed in the morning.

Results: Concerning after-effects, subjectively evaluated sleep quality decreased and reaction time ascertained for a switch task increased with noise levels. Most physiological variables revealed, however, the same reactions to both the lower noise levels and considerably stronger responses to the highest noise load. Event-related awakenings increased gradually with maximum noise levels and were highest for rail and lowest for road noise. Slow-wave sleep was most delayed and reduced during nights with railway the least during nights with road noise where subjective evaluation and performance showed no differences.

Conclusions: The equivalent noise level seems to be a suitable predictor for subjectively evaluated sleep quality but not for the physiological disturbances of sleep as road-, rail- and aircraft noise caused the same after-effects but concerning the physiological indicators deep sleep was most severely affected by rail noise.

TS 03.05
The relevance of noise sensitivity for sleep, subjective sleep quality, and mood after noise disturbed nights

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Aims: The study examines the relationship between noise sensitivity and sleep, subjective evaluation of sleep as well as mood under the influence of nocturnal traffic noise exposure. It was hypothesized that noise sensitivity enhances the negative impact of traffic noise during the night on the aforementioned variables.

Methods: A total of 24 healthy and normal hearing students (12 male, 12 female) with age ranging from 20 to 29 years took part in the study. After an adaptation night they slept over a period of 3 consecutive weeks in the laboratory. In each week they spent 4 consecutive nights in the laboratory. The participants were exposed to traffic noise during three nights of each week (road-, rail- and aircraft noise with equivalent sound levels of Leq=39, 44 and 50 dBA) where the forth quiet night was randomly inserted with a background noise of 32 dBA. The polysomnogram
(2 EEG, 2 EOG, 1 EMG) was recorded continuously throughout all nights. Sleep quality (6 ten-point scales measuring difficulties to fall asleep, calmness of sleep, sleep depth, sleep duration, recreation, and body movements) and mood (3 ten-point scales) were evaluated after awakening. Noise sensitivity was measured using the NoiSeQ (Noise-Sensitivity-Questionnaire, Schütte & Marks 2004), which contains 35 items.

Results: The polysomnogram was evaluated applying the criteria of Rechtschaffen and Kales (1968). Correlations were calculated between individual noise sensitivity and physiological sleep data as well as subjective evaluation of sleep, based on data averaged over all nine noisy nights. Concerning correlation coefficients subjective sleep quality decreased with increasing noise sensitivity (calmness r= .324 p=0.061; recreation r=.276 p=0.096; body movement r=.434 p=0.017). Objective sleep parameter as derived from the polysomnogram and mood revealed no significant correlations with individual sensitivity to noise.

Conclusions: Relationships were found between physical traffic noise exposure, individual sensitivity to noise and subjective response in terms of worsened sleep quality. Subjective responses of nocturnal noise are not only influenced by physical parameters of the noise itself but also by individual factors. In this sample objective sleep data did not predict subjective evaluation of sleep.

TS 04: Recent advances in REM-behaviour disorders

TS 04.01
Diagnosis and Differential Diagnosis of Rapid Eye Movement (REM) Sleep Behaviour Disorder (RBD)

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RBD is a disorder primarily of older males with abnormal behaviours during REM sleep causing injury or sleep disruption, usually from the acting-out of stereotypically altered dreams featuring confrontation, aggression, and violence—without daytime tendency for increased aggressiveness. The diagnosis of RBD is established by its clinical history and by documenting with electromyographic monitoring during polysomnography (PSG) the presence of increased muscle tone &/or phasic muscle twitching during REM sleep. Periodic limb movements during NREM sleep (usually without arousals) are very common, and there is increased sleep delta power and slow-wave sleep for age. Waking EEG shows slowing compared to controls; neuropsychological testing shows visuospatial constructional dysfunction and visuospatial memory impairment; and there is olfactory dysfunction. Thus, RBD is a global disorder of REM sleep, NREM sleep and wakefulness and is commonly associated with narcolepsy, parkinsonism, stroke & other brain disorders. In one series, 65% of men >50 yrs old initially diagnosed with idiopathic RBD eventually developed parkinsonism at a mean interval of 13 years. Differential diagnosis of dream-enacting behaviors includes disorders of arousal, obstructive sleep apnea, nocturnal seizures, etc. RBD is the only Parasomnia in the recently published International Classification of Sleep Disorders-2 that requires PSG monitoring for its diagnosis.

TS 04.02
RBD: Mechanisms responsible for the suppression of muscle tone in sleep

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REM sleep without atonia results from a disruption in the normal balance between motor excitation and inhibition in REM sleep. The motor inhibition results from both disfacilitation and active inhibition. Disfacilitation results from the reduction in serotonergic and noradrenergic facilitatory influences. These in turn are under the control of brainstem GABAergic and other mechanisms. Histaminergic neurons despite having a sleep cycle discharge pattern similar to that of noradrenergic and serotonergic cells do not appear to participate in motor disfacilitation but rather are linked to maintenance of waking awareness. Active inhibition of motoneurons during REM sleep results from increased release of GABA and glycine on to motoneurons. Hypocretin neurons have an important role in coordinating these systems controlling muscle tone.

TS 04.03
Neuroimaging in REM behaviour disorder

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Physiologically spinal motoneurons are inhibited during REM sleep via the nucleus reticularis magnocellularis
(NRMC) which receives excitatory afferences from the periventricular region (peri-LC region). Animal models show that bilateral pontine lesions particularly in the peri-LC region cause REM sleep without atonia (RSWA) typical for RBD. In addition, the pedunculopontine nucleus (PPN) and the ventral mesopontine junction (VMPJ) have been shown to be specifically involved in RBD pathophysiology. An increasing number of studies shows that RBD is associated with alpha-synucleinopathies. Longitudinal studies from Schenck et al. identified 38% of 29 patients with RBD who subsequently developed a parkinsonian disorder after 12.7 years. A further follow-up study demonstrated that 65% developed parkinsonism and/or dementia. Cross sectional studies in patients with Parkinson’s disease (PD) show that 33% of PD patients have RBD and 58% subclinical RBD (RSWA). IPT-SPECT studies also revealed a reduced dopamine transporter binding in patients with ‘idiopathic’ RBD in terms of presymptomatic PD (Eisensehr et al. Sleep 2003). The new staging of PD based on neuropathological analysis using synuclein immunohistochemistry (Braak et al. Neurobiology of Aging 2003) revealed striking overlap between the presumed brainstem nuclei involved in RBD and PD pathophysiology. According to the Braak classification Lew bodies (aggregated alpha-synuclein) are found initially in the IX/X motor nucleus and the olfactory nucleus/bulb (stage 1). In stage 2 additional lesions are found in the medulla and the pontine tegmentum (NRMC, coeruleus and subcoeruleus region). Only in stage 3 the PPN and the substantia nigra are affected. Synuclein pathology finally ascends to more rostral and cortical structures (stage 4–6). This temporal sequence of synucleinopathy could explain why RBD precedes PD (stage 3) and dementia (stage 4–6). The finding that 97% of patients with RBD have hyposmia (Stiasny-Kolster et al. Brain 2005) is also in line with the Braak staging (stage 1). Accordingly, the clinical symptoms hyposmia and RBD have to be considered as early symptoms of Parkinson’s disease. RBD has also been shown to be associated with multiple system atrophy (MSA) or dementia with Lewy bodies (DLB), other neurodegenerative diseases which share the similarity of alpha-synuclein positive intracellular inclusions. In contrast, RBD is not or rarely associated with tauopathies (e.g. Alzheimer’s disease, progressive supranuclear palsy or corticobasal degeneration).

TS 05: Sleep disordered breathing in children

TS 05.01
The Epidemiology of Sleep-Disordered Breathing in School-Aged Children

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Background: Little is known about the prevalence, expression, risk factors, and neurocognitive consequences of sleep-disordered breathing (SDB) in primary school children. We aimed to investigate these aspects using a population-based epidemiological approach.

Methods: An explorative population-based cross-sectional study in 1144 third grade pupils was performed. Parents were asked to fill in a 25-item questionnaire concerning symptoms of SDB; children underwent nocturnal home pulse oximetry. Children presenting with abnormal results in either test modality subsequently underwent nocturnal home polysomnography.

Results: The prevalence of habitual snoring and obstructive sleep apnea hypopnea syndrome was found to be 10.0% and 2.8%, respectively (95% confidence interval (CI): 8.2–11.7 and 1.8–3.8). The prevalence of non-apneic habitual snoring (i.e. habitual snoring without evidence of apneas and/or hypopneas) was 6.4% (5.0–7.8). Habitual snoring was an independent risk factor for poor academic performance in mathematics (odds ratio, 95% CI: 2.7; 1.5–4.9), science (2.4; 1.2–4.8), and spelling (2.3; 1.3–4.1). Non-apneic habitual snoring, but not obstructive sleep apnea hypopnea syndrome, was significantly associated with poor academic performance in mathematics (2.4; 1.4–4.4), science (2.7; 1.4–5.0), and spelling (2.5; 1.4–4.5).

Conclusions: This study adds evidence that SDB may be a frequent entity in children and may lead to neurocognitive impairments. It also suggests that mild expressions of SDB may result in such impairments as well. Identification of risk factors may help to detect children at risk for SDB.

TS 05.02
Effects of Intermittent Hypoxia on Cognitive Functioning in Children

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Obstructive sleep apnea syndrome (OSA), the most severe form of sleep disordered breathing (SDB), is a frequent medical condition in which the upper airway becomes blocked repeatedly during sleep, resulting in intermittent hypoxia (IH) and sleep fragmentation resulting from the recurrent arousals from sleep necessary to relieve the upper airway obstruction. The morbid consequences of untreated OSA primarily include cardiovascular, metabolic, and neurocognitive dysfunction. Given the increasing prevalence of pediatric OSA, it is therefore essential
to identify the neurobehavioral effects of the disease in this population. Children with OSA display inattention, impulsivity, emotional dysregulation, poor academic achievement, aggression, and overall behavioral maladjustment more often than their peers. Although the mechanisms underlying such neurobehavioral impairments in children remain to be elucidated, data from rodent models suggest that IH plays a substantial role in OSA-associated neurocognitive morbidity. Exposure to experimentally-induced IH in the rat is associated with age-related neurodegenerative changes and alteration in brain regions and neurotransmitter systems involved in learning and memory, as well as attention and locomotor activity. Multiple cellular and molecular mechanisms have been implicated in the neurobehavioral morbidity associated with IH during sleep, and include such factors as increased oxidative stress, up-regulation of pro-inflammatory mediators, as well as altered regulation of pro- and anti-apoptotic gene cascades. Collectively, the available data indicate that exposure to IH during sleep is associated with adverse behavioral and neuronal consequences in the rodent which are more pronounced in the juvenile animal, and may have important developmental implications for clinical populations.

TS 05.03
Treatment of OSAS in children: nasal CPAP
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Home nasal CPAP has been used in infants, pre-pubertal children, and pubertal children. The first report of its usefulness in children in 1986 was a prospective study that followed 5 children, age 3 to 11 years, for 10 months (Guilleminault et al). Similar findings were reported in several large retrospective studies (Waters et al, Marcus et al, Guilleminault et al, Rains, McNamara and Sullivan, Downey et al). These studies primarily involved children older than 12 months of age. Infants 8 to 18 weeks of age were followed from the onset of treatment through the first 12 months of age in a study in 1995; (Guilleminault et al) this was replicated in 1999 (McNamara and Sullivan). The difficulty in application of nasal CPAP relates to training of the family and child as well as finding the appropriate nasal interface. Children often need to be trained to tolerate the facial interface; behavioral modification techniques and daytime training may help with this training. 1. CPAP is very useful when the SDB is related to major craniofacial deformities or other illnesses. If the upper airway problem is complicated by neuromuscular disease, nasal bilevel may be used. Regular follow-up should be performed within the first three months to evaluate mask fitting. Due to rapid craniofacial growth of young children, CPAP pressure should be evaluated every 6 months. An annual craniofacial specialist visit should occur to affirm that headgear and mask do not worsen a maxillary growth deficiency (Li et al). Clinicians should encourage the use of humidification, aggressively treat allergies and/or rhinitis and check nasal patency. An obstructed nose will be responsible for failure of acceptance of nasal CPAP and a systematic, in depth evaluation of the nose if necessary with rhino-fibroscopy will help improve children tolerance to equipment. One major difficulty is to assess properly the nose of a young uncooperative child: between 20 and 80% of deviated septum has been reported to be congenital and allergies are common by one year of age and contribute to sleep disordered breathing Usage of nasal steroid may not be sufficient and performance of reduction of nasal inferior turbinates with radio-frequency with appropriate monitoring of temperature and performance of the procedure by an experienced pediatric ENT trained in this procedure can be helpful. Such procedure may need to be done under sedation in younger children. In light of children’s favorable response to surgery with or without orthodontic and anti-allergic treatment, nasal CPAP should only be a second consideration.

TS 05.04
Rapid Maxillary Expander in the Treatment of Ostruc-tive Sleep Apnea Syndrome (OSAS) in Children
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Aims: The craniofacial dysmorphism leads to OSAS may involve a delayed growth of the mandible that induces a mandibular retroposition (MR). MR is associated with posterior displacement of the tongue base. A high arched palate is also common in patients with OSAS. The orthodontic approach could play an important role in the management of snoring and OSAS children. (Villa et al, Am J Resp Crit Care Med 2002- Pirelli et al. Sleep 2004) .Unfortunately poor data are available on efficacy and long term outcome. Aim of the study was to evaluate efficacy of a Rapid Maxillary Expander on 12 months trial in OSAS children.

Methods: We studied 25 OSAS patients (mean age 6.2 ± 2.5; 16 males),with deep, retrusive or crossbite. Exclusion criteria were obesity and other cardiopulmonary diseases.16 patients were randomly assigned to undergo a 12-mo RME treatment, the remainig 9 subjects (6.0 ± 2.1; 5 males) acted as a control group. Each patient underwent to standard overnight polysomnography (PSG): baseline, after six and twelve months of treatment.

Results: Two patients dropped out at the second PSG respectively for rapidly gain weight (BMI 32) and recurrent asthma. Our results showed that RDI score and clinical
symptoms decreased significantly in treated subjects at the end of treatment (5.8 ± 6.8 vs 1.6 ± 1.7; p = 0.007) respect to untreated subjects (2.7 ± 4.9 vs 2.5 ± 3.2; p = ns). The RDI score decreased more in children with OSAS and deep or retrusive bite (6.6 ± 6.0 vs 1.1 ± 1.2; p = 0.005) compared to those with crossbite (4.3 ± 2.0 vs 2.5 ± 2.1; p = 0.004). Arousal Index was normalized in treated subjects (6.1 ± 8.7 vs 0.1 ± 0.4; p = 0.001) respect to untreated (4.8 ± 2.6 vs 4.5 ± 1.5).

**Conclusions:** Rapid Maxillary Expansion may be a useful approach in children with malocclusion and OSAS.

**TS 06.01**  
The interaction of sleep and the hypothalamo-pituitary adrenocortical system in pathophysiology and therapy of affective disorders

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**Aims:** Dysregulation of several endocrine and neurotransmitter systems are involved in the pathophysiology of depression. Changes in the activity of the renin-angiotensin-aldosterone system (RAAS) and the hypothalamicpituitary-adrenocortical (HPA) have been reported. Therapeutic sleep deprivation has rapid antidepressive efficacy in some patients. We were interested if and how these pathways react to sleep deprivation.

**Methods:** We used polysomnography and analysed the serum concentrations of several hormones in the course of the night to determine hormone concentrations in healthy subjects and patients with depression before and after one night of total sleep deprivation (TSD). Furthermore we performed an analysis by means of NMR spectroscopy of intracerebral GABA, glutamine and glutamate in healthy subjects before and after TSD. For the polysomnographic studies we compared the sleep related activity of RAAS and HPA hormones before and after TSD in seven depressed patients. After an accommodation night a polysomnographic examination was performed between 23.00 h and 7.00 h. This was followed by 40 h of TSD and the second polysomnography. During the examination nights blood samples were taken every 20 min for analysis of renin, aldosterone, ACTH and cortisol. The NMR spectroscopic analysis was performed with 7 healthy controls in the morning of the first day and again 24 h later. An increase in GABA and glutamine levels in pontine areas was observed.

**Results:** During recovery-sleep renin was significantly increased (p<0.05). Aldosterone showed no change. ACTH and cortisol were decreased by trend in the first half of the night. REM-density and intermittent wakefulness was significantly decreased (p<0.05), whereas slow wave sleep increased by trend in the first half of the night. TSD in patients with depression leads to changes, which are in accordance with a desensitisation of angiotensin II receptor sensitivity. The MR-spectroscopic studies revealed an increase in GABA and glutamine levels in pontine areas.

**Conclusion:** It is known that angiotensin via ATII receptors and glutamate act synergistically to increase the HPA axis activity whereas GABA reduces it. As a reduction of HPA axis activity is accompanied by a clinical improvement in hypercortisolemic patients these findings are in line with the hypothesis that the same group of patients might benefit from therapeutic sleep deprivation.

**TS 06.02**  
Contribution of microsleep and GABAergic neurotransmission to disturbed sleep wake regulation in depression and antidepressant response

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Sleep deprivation (SD) has an antidepressive, but temporary efficacy in about 60% of depressed patients. Characteristic sleep-EEG alterations of depression are improved after SD in the recovery night. Naps and short sleep-episodes (microsleep) during SD reduce NonREM sleep pressure in the recovery night. Furthermore, early morning naps and microsleep during SD can prevent the antidepressant effect of SD. The GABA-A-benzodiazepine receptor antagonist flumazenil reduces daytime-sleep and increases vigilance. In addition, flumazenil is able to suppress NonREM sleep pressure in early morning recovery sleep after SD in healthy subjects, which is the critical time for a detrimental effect of microsleep and naps on sleep deprivation response. Based on these findings, either flumazenil or placebo was orally applied during the initial hours of partial sleep deprivation (PSD) in patients with major depression (MD). The application of flumazenil significantly reduced microsleep compared to placebo, predominantly in the first part of PSD when flumazenil was applied. In the recovery night under flumazenil sleep continuity improved, stage 1 was significantly reduced and slow wave sleep significantly increased compared to placebo. These findings show that flumazenil is able to suppress MS during PSD in depressed patients. The suppression of MS seems to be related to an increased NonREM sleep pressure in the recovery night reflected by
decreased stage 1 and increased SWS. The different effects between flumazenil and placebo in the recovery night suggest that GABAergic mechanisms are substantially involved in sleep-wake regulation in depression and may probably contribute to the sleep deprivation response in MD.

TS 06.03
Antidepressant induced alteration of sleep EEG as a surrogate marker of drug activity: a window to the neurobiology of depression

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Dysfunctions of the central monoaminergic system have been implicated in the neurobiology of depression and since both serotonin and noradrenaline are involved in sleep regulation processes, it has been proposed that sleep EEG alterations observed during major depression could reveal these monoaminergic dysfunctions. In the present study, we investigate whether the effects of a serotonergic antidepressant (citalopram) on sleep EEG parameters could be differentiated from those of a noradrenergic antidepressant (reboxetine). These effects were compared relative to those of placebo and of a non antidepressant drug enhancing noradrenergic transmission (yohimbine). 16 healthy male volunteers aged 27±6.3 years were included in a double-blind placebo-controlled 4-way cross-over study including 4 sessions each separated by at least a 8-day wash-out period. Each subject received either citalopram 40 mg, reboxetine 8 mg, yohimbine 40 mg or placebo. Difference from baseline values were analyzed on the per protocol set allowing for subjects, sequence, periods and treatment. The results of the present study demonstrated the dramatic effects of a single administration of citalopram or reboxetine on sleep -continuity-,architecture and -profile in comparison to those induced by yohimbine. Both antidepressant drugs displayed REM suppressing properties but differed in terms of their effects on wake propensity. The effects of yohimbine were modest and consisted of a sleep disrupting effect comparable to those of reboxetine but without influence on REM sleep. The present results study bring some support to the idea that polysomnographic recordings could distinguish noradrenergic from serotonergic reuptake blocking properties of an antidepressant drug.

TS 06.04
Sleep EEG and HPA axis regulation changes under antidepressant treatment and prediction of response

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Aims: In the majority of depressed patients neurobiological alterations are well documented findings i.e. dysregulation of hypothalamic-pituitary-adrenocortical (HPA) system function and/or characteristi-c alterations in EEG sleep measures like disturbed sleep maintenance, a deficit of slow wave sleep (SWS) especially during the first sleep cycle, an earlier onset of the first rapid eye movement (REM) sleep period (shortened REM latency), and increased density of REM during REM sleep (REM density). However, the course and the predictive value of these alterations for treatment outcome as well as for long-term course of depression still warrants clarification. Therefore, we examined whether (1) the previous clinical course of depression, (2) treatment response during a standard antidepressant therapy, and (3) the long-term outcome in follow-up are associated with abnormal EEG sleep para-meters. Since the hypothalamic-pituitary-adrenocortical (HPA) system seems to play a crucial role in treatment outcome and course of depression, we evaluated HPA system function as well.

Methods: 15 patients (4 men, 11 women; age 43–59) with major depression (ICD-10: F31, F32 or F33) without psychotic features were consecutively enrolled in the study. HPA system assessment using the combined DEX/CRH test and sleep EEG studies were conducted at baseline, after a 6 week treatment period with a standard antidepressant (trimipramine 200 mg/d), and at follow-up after long-term course i.e. after 2 to 10 years after remission of the index episode. Recurrence rates re-flected as proportion between number of recurrences and time between baseline investigation and reevaluation constituted the major outcome variable.

Results: 1. The previous clinical course as reflected by the number of episodes until baseline corre-lated significantly with EEG sleep measures i.e. sleep continuity values, and SWS (Spearman’s rho: r = -.59, p < 0.05). 2. During treatment sleep continuity values improved and the correlation with the previous long-term course disappeared. However, the correlation with SWS persisted (r = -.52, p < 0.05). 3. In the prospective long-term outcome SWS (r = -.61, p < 0.05) and REM density (r =.61, p < 0.05) variables were related to the occurrence of recurrences in follow-up. These identified sleep EEG markers correlated closely with HPA system regulation. SWS values showed a negative (r between −0.51 and −0.62, p < 0.05) and REM density a positive correlation (r between 0.41 and 0.60, p < 0.05) with increased HPA activity.

Conclusions: SWS, especially during the first sleep cycle, and REM-density are of predictive value for the long-term course of major depression. Furthermore, these sleep alterations are closely related to HPA system dysregulation.
This finding is in accordance with the extended neurophysiological-neuroendocrinological two process model of sleep regulation and its implication for depression.

**TS 07: Objective Measurement of Sleepiness in Patients with Mood and Sleep Disorders**

**Aims:** Immersion of a person into psychophysiological model of stress situation similar to theirs’ professional one clearly reveals impairment of performance abilities, especially if biofeedback technology is conjunct.

**Methods:** Subjects of the study were locomotive drivers (15 males of age 26–32, railroad managers (14 males of age 28–36). Cardiointerval game-like biofeedback sessions (“VIRA!” and “RALLY”) were performed as a stress-test: there was an obligatory goal-one had to win. Session of “VIRA!” consisted of 5–7 trials. A successful performance of the test depends on the heart rate control skill. “RALLY” lasted also 15 minutes and consisted of 5 trials. In this test attention concentration level was registered which was determined by the latent response time on obstacles appearing occasionally on the racer’s way (RT). Standard psychological inventory and CPT tests were applied.

**Results:** Each group was homogeneous in all physiological characteristics, as well no significant psychophysiological distinctions were revealed between groups. Principal component analysis of effectiveness coefficients, ANS balance indicators made it possible to separate group of high performance from the poor one. The main asset into the classification procedure has been done by RALLY factor, RT had the highest scores. Somnolence correlated with RT significantly (p<0.01) as well.

**Conclusions:** Performance impairment and somnolence can be assessed by RALLY with high grade of reliability.

**TS 07.02**

**Psychological Correlates of the Ability to Overcome Drowsiness and Stress Throughout Biofeedback Training**

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**Aims:** The study is aimed on validation of the system (“RALLY”) for enjoyable relaxation training. This system combines a biofeedback device, alertness test, computer game, and non-invasive detector of imbalance in autonomic tone.

**Methods:** The psychological states and performance were evaluated in 25 subjects aged between 18 and 26 years before and after biofeedback relaxation training. Every subject completed 10 30-min relaxation sessions divided by 1–3-day intersession intervals. To learn the art of relaxation, the subject must succeed in the on-screen competition between two drivers. The main (relaxation) task is to accelerate the on-screen car by slowing down subject’s heart rate. The additional (performance) task is to react as quickly as possible on the randomly appeared obstacles (rocks on the on-screen road).

**Results:** The pretreatment performance significantly correlated with the levels of depression (p<0.05), and anxiety (p<0.05). The training led to the significant reduction of the levels of neuro-psychic tension (p<0.001), depression (p<0.01), and anxiety (p<0.001). The success in relaxation training significantly correlated with the dynamics of neuro-psychic tension (p<0.05), and the improvement in performance significantly correlated with the dynamics with both neuro-psychic tension (p<0.05) and anxiety (p<0.05).

**Conclusions:** The RALLY can serve as a tool for objective measurement of sleepiness level and performance impairment in the course of relaxation training. The relaxation training is associated with considerable benefits for both psychic and physiological functioning.

**TS 07.03**

**Sleepless in Alaska and Siberia: Cross-validation of factor structure of the individual adaptability of the sleep-wake cycle**

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**Background:** Some results of psychometrical evaluation of chronotypological questionnaires point on the multidimensional nature of the adaptive ability of individual sleep-wake cycle. However, the exact factor structure of this ability and the physiological factors underlying the variety of subjectively assessed individual traits of the sleep-wake cycle still remain to be clarified. The study was designed to cross-validate the factor structure of the sleep-wake adaptability and to suggest a model explaining its multidimensional nature.

**Method:** The English and Russian versions of 4 chronobiological questionnaires (Horne, Åstberg, 1976;
Folkard et al., 1979; Putilov, 1987, 1990, 1997) were administered to 160 students of the University of Alaska Anchorage and to 180 students of the Novosibirsk State University, respectively.

Results: The factorial structures of the English and Russian versions of the questionnaire were found to be almost identical. The psychometrical analysis revealed a hierarchical structure with 3 superfactors on the top of this hierarchy. The suggested physiological model predicts that the hierarchical multi-dimensional structure of the sleep-wake adaptability might be produced by combination of just three underlying physiological factors.

Conclusion: The results suggest that the subjectively assessed features of the sleep-wake cycle reflect the underlying inter-individual differences in the mechanisms of chronophysiological regulation.

TS 07.04
Placebo Controlled Melatonin Treatment of Hypersomnic Winter Depression Following Sleep Deprivation with EEG Recording

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Aims: Sleepiness can be objectively measured by spectral analysis of the waking electroencephalogram (EEG) in the 1–10 Hz band. We tested whether normal build-up of sleep pressure is attenuated in hypersomnic winter depressives during prolonged wakefulness and whether subsequent early evening melatonin administration stabilizes their mood and improves their sleep habits.

Methods: The waking EEG was measured every 3 hours in 16 female patients with winter depression and 13 age-matched healthy controls throughout a total sleep deprivation for 30 hours. Melatonin or placebo under double blind conditions was administered subsequently (0.5 mg at 17:00 for 6 days), and, thereafter, the waking EEG was partially reassessed (for 12 hours).

Results: The increase of EEG power density at 5–5.99 Hz, derivation Fz-Cz, during 30-hour wakefulness was significantly attenuated in patients compared to controls (p = 0.037 for difference between linear trends). Subjective sleepiness and energy self-ratings confirmed the difference in EEG dynamics (p = 0.092 and p = 0.045, respectively). Although mood was stabilized by subsequent treatment with melatonin or placebo, the habitual sleep timing was not altered, and no differential antidepressant effect of melatonin or placebo was observed.

Conclusions: Overall, the patients manifest the same wake EEG characteristics as long sleepers (i.e. an impaired homeostatic component of sleep regulation). Although melatonin treatment was appropriately timed to phase advance circadian rhythms, it did not prove its antidepressant and sleep advancing efficacy over placebo.

TS 08: New developments in the treatment of sleep disturbances in the elderly

TS 08.01
Sleep Problems in the Older Adults and the Effects of Aerobic Training

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Significant sleep disturbance is an extremely common complaint in older adults. Epidemiological studies show that approximately half of older adults complain of significant and frequent sleep disturbance and as much as six percent of the older population may suffer with a diagnosable insomnia. The major causes of sleep disruption in aging include: (1) physiological changes that arise as part of normal, “non-pathological” aging; (2) sleep problems due to physical or mental health conditions and their treatment; (3) primary sleep disorders; (4) poor “sleep hygiene” or sleep-related habits; or, (5) some combination of these factors. Regular exercise, typically a component of any sleep hygiene prescription, is assumed to improve sleep quality. We briefly review these various causes of sleep disturbance in older adults and examine the data supporting the usefulness of exercise, specifically regular endurance or aerobic exercise as a treatment for sleep disturbance in community-dwelling older adults. The epidemiological and experimental literature will be reviewed and initial results of a recently completed randomized controlled trial of endurance training in a sample of sleep-complaining, community-dwelling older adults reported.

TS 08.02
Effects of Bright Light Treatment

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Aims: Sleep disturbances are common in the elderly, especially among patients with dementia living in institutions. It has been suggested that age-related changes in sleep may partly reflect fundamental changes in the circadian timing system. The hypothalamic suprachiasmatic nucleus is considered to be the principal component of the circadian timing system and essential in the synchronisation
of internal rhythms with external time-cues, like the environmental light-dark cycle. Bright light treatment has been reported to reduce sleep disturbances and improve circadian rhythm parameters in nursing home patients. We will here present data exploring the effects of bright light exposure in demented nursing home patients with sleep disturbances.

Methods: We will mainly present data from a study where bright light treatment was given for 2 hours/day in the morning for two weeks. Both subjective (nursing staff observations) and objective (actigraphy) data will be presented. Data were obtained during pretreatment and treatment weeks, as well as at four monthly post-treatment periods.

Results: Sleep at night improved substantially with treatment; sleep efficiency increased from 73% to 86% and total nocturnal wake time was reduced by nearly two hours. During the 16 weeks post-treatment period, actigraphic measures gradually returned to pretreatment levels. Sleep efficiency remained significantly higher than the pretreatment level four weeks after treatment termination. Sleep onset latency remained significantly reduced up until 12 weeks post-treatment. In addition, daytime wakefulness was increased. This improved daytime wakefulness was however short-lived, and did not last into the first post-treatment period after 4 weeks.

Conclusions: These data support the beneficial effects of bright light therapy for sleep disturbances in demented nursing home patients. Furthermore, morning bright light exposure increases daytime wakefulness. The effects of bright light on sleep at night last for several weeks post-treatment, whereas the effects on daytime wakefulness are short-lived.

TS 08.03
Long-Term Outcomes Following Benzodiazepine Discontinuation and Cognitive-Behavior Therapy in Older Adults with Insomnia

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Background: Both insomnia and hypnotic use increase with aging. Discontinuation of benzodiazepine (BZD) treatment for insomnia can be a difficult task for some patients. Several studies have shown that a supervised medication taper, combined with cognitive-behavior therapy (CBT) for insomnia, can facilitate withdrawal but there is limited information on long-term outcome after discontinuation.

Methods: The objective of this study was to examine medication-free survival time and predictors of relapse (i.e., resumed BZD hypnotics) over a 2-year period. The sample consisted of 47 older adults (mean age 62.1 years) with persistent insomnia and prolonged BZD use (average duration of 18.9 years), who had successfully discontinued BZD following a supervised medication taper program, CBT for insomnia, or a combined approach. The Kaplan-Meier product-limit method was used to estimate survival time, defined as time between end-of-treatment and relapse or end of follow-up.

Results: By the end of the 24 month follow-up, 42.6% of the sample had resumed BZD use. Relapse rates were significantly lower in the Combined (33%) and Taper (31%) groups relative to the CBT group (69%). Survival rates at 3 months were 81% (Combined), 100% (Taper), and 61.5% (CBT). At 12 months, they were 83%, 71%, and 39%, respectively; and, at 24 months, they were 65% for both the Combined and Taper groups and 29% for CBT. Mean survival time was significantly longer for both the Taper (18.6 months, SE=2.1) and Combined groups (12.6 months, SE=1.4), relative to the CBT group (8.5 months, SE=1.8). Significant predictors of relapse included perceived insomnia severity, psychological distress, using more than one BZD, and taking more time to discontinue BZD. Age, gender, and the occurrence of lapses were not predictive of relapses.

Conclusions: Although CBT may facilitate initial BZD discontinuation, the addition of a supervised medication taper enhances long-term outcome. Nonetheless, there is a substantial relapse rate following BZD discontinuation among prolonged users and long-term maintenance strategies may be necessary to prevent relapse.

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TS 08.04
Psychological treatment in the management of chronic insomnia in primary care: a service delivery model

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Patients presenting, or recalled, for repeat hypnotic prescriptions in 23 Sheffield general practices were invited to participate in either the clinic (50%) or control (50%) conditions of the study. Clinic patients were offered a package of evaluated psychological therapies for insomnia over 6 sessions. Treatment was delivered by primary care counsellors supervised by a clinical psychologist. Controls were assessed, but received no additional treatment. Outcomes included sleep quality, drug use, and patient ratings of service satisfaction. Economic analyses of trial costs and NHS insomnia care were conducted alongside the trial. A total of 108 and 101 patients (age range 31–92 years) participated in the clinic and control groups respectively.
The sleep clinic was associated with significantly improved sleep quality, significantly reduced hypnotic use, positive ratings of patient satisfaction, and high take-up by general practices. Economic analyses indicated substantial hidden costs associated with hypnotic drug usage. Treatment outcomes were independent of patient age.

TS 09: Narcolepsy 2005

TS 09.01
Behavioral role of hypocretin (orexin)

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TS 09.02
Pathophysiology of cataplexy

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Cataplexy the only specific symptom of narcolepsy- is characterized by a bilateral loss of muscle tone in response to emotional stimuli. Although the combination of a sudden paralysis with preserved consciousness, which is triggered by emotions has fascinated physicians for a long time, the pathophysiology of cataplexy is still largely unknown. The pattern of muscle weakness and the fact that narcolepsy is associated with Sleep Onset REM Periods gave rise to the hypothesis that cataplexy is a dissociated expression of the atonia that usually accompanies REM sleep. Although cataplexy is mediated by certain brainstem structures that do play a role in the regulation of REM sleep, there are several arguments against the REM-dissociation hypothesis, both on pharmacological and on neurophysiological grounds. In the last couple of years, it has been shown that human narcolepsy is associated with defects in hypocretin neurotransmission, which are reflected in undetectable levels of hypocretin-1 in the cerebrospinal fluid. Strikingly, this hypocretin deficiency is limited to those patients who have cataplexy. Furthermore, studies measuring the activity of hypocretin neurons in freely moving rats show the highest neuronal firing rates during high-intensity exploratory behaviour. Finally, hypocretin neurons not only have connections to various brainstem nuclei, but also project directly onto spinal motorneurons. Taken together, these data suggest that the hypocretin system acts at multiple levels to suppress the unwanted onset of atonia which is associated with strong emotions even in healthy subjects. Defects in this system may then result -besides the other symptoms of narcolepsy- in the emergence of cataplexy.

TS 09.03
Diagnosis of narcolepsy

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TS 09.04
Treatment of narcolepsy

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TS 10: Beyond AHI: New Approaches for Quantifying Sleep Related Breathing Disturbances

TS 10.01
Beyond the Apnea/Hypopnea Index

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Introduction: Sleep disordered breathing is a complex disorder characterized by upper airway obstruction and concomitant reductions in ventilation, which lead to sleep disruption and oxyhemoglobin desaturation. The apnea/hypopnea index, a primary metric for sleep apnea severity, does not accurately describe the disturbance in upper airway obstruction and ventilation during sleep. We hypothesized that disturbances in upper airway function and ventilation during sleep can be characterized with quantitative measurements of airflow during sleep.

Methods: Pressure-flow relationships were described in weight, age and gender-matched groups of normal and sleep apnea subjects. These relationships were analyzed to determine the degree to which upper airway anatomy contributes to development of airway obstruction during sleep (as reflected by critical pressure measured under conditions of low neuromuscular tone). Neuromuscular responses to upper airway obstruction were characterized by measuring the changes in airflow, inspiratory duty cycle and respiratory rate in response to experimentally-induced periods of upper airway obstruction during sleep.

Results: Patients with sleep apnea were characterized by elevations in passive Pcrit, indicating that anatomic defects predispose to obstructive sleep apnea in this group compared to normal individuals. In contrast, experimentally-induced periods of upper airway obstruction during sleep were associated with greater increases in airflow in normal compared to sleep apnea subjects. Female gender and obesity were associated with baseline elevations in inspiratory duty cycle, which limits the ability of these
subjects to compensate for upper airway obstruction with a prolongation of inspiration.

**Conclusions:** Obstructive sleep apnea is associated with disturbances in both upper airway anatomy and neural control, and compensatory responses in respiratory pattern can mitigate upper airway obstruction and decrease susceptibility to sleep apnea.

**TS 10.02**
**New methods for assessing respiration during sleep**

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Respiratory disturbances in patients with the obstructive sleep apnea/hypopnea syndrome are characterized by recurrent reductions in ventilation and increases in inspiratory efforts caused by abnormally high upper airway resistance. Given that recording flow by a pneumotachograph demands the use of a nasal mask, in routine sleep studies ventilation is semiquantitatively assessed by thermistors/thermocouples. To noninvasively estimate inspiratory efforts thoraco-abdominal bands are commonly employed. Routine assessment of airway resistance is difficult because the reference method requires the use of an esophageal balloon. However, new methods have been developed in recent years to facilitate the assessment of respiration during sleep. For instance, quantitative assessment of flow amplitude and detection of flow limitation are possible by using nasal prongs. Moreover, inspiratory efforts can be noninvasively monitored by means of the pulse transit time technique. Finally, two methods allow the assessment of upper airway obstruction in a way that is noninvasive and does not disturb the patient’s sleep: the measurement of the upper airway critical pressure and the forced oscillation technique. Although their application is mostly restricted to clinical research to date, these new methods to assess respiration during breathing are potentially useful in routine sleep studies.

**TS 10.03**
**Breath-wise approaches to the assessment of inspiratory airflow limitation during sleep**

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**TS 10.04**
**New approaches to the development of composite respiratory phenotypes during sleep**

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**Conceptual Approach:** We examined the effect of gender on respiratory phenotypes for obstructive sleep apnea. Respiratory phenotypes were derived from the classical relationship: $VT = (VI) \times (TI/TTOT) \times TTOT$, where $VT$ is the inspired tidal volume, $VI$ the mean inspiratory airflow, $TI/TTOT$ is the inspiratory duty cycle, and $TTOT$ is the length of the respiratory cycle. During periods of upper airway obstruction, inspiratory flow is limited to a maximal level that cannot be exceeded as effort increases. Therefore, in the presence of upper airway obstruction, patients can defend inspiratory tidal volume only by prolonging either inspiratory duty cycle or the length of the respiratory cycle.

**Methods:** We induced upper airway obstruction with inspiratory flow limitation during NREM sleep by exposing male and female patients without obstructive sleep apnea, matched by age (8 years) and BMI (3 kg/m²), to subatmospheric nasal pressure. The mean inspiratory airflow was used to define three distinct levels of upper airway obstruction (UAO), based on the mean inspiratory airflow of 175–225 ml/s (mild), 125–175 ml/s (moderate) and 75–125 ml/s (severe).

**Results:** Eleven subjects were identified in each gender group, with mean age 33.6 years (SD 10.0 years) and BMI 27.0 kg/m² (SD 3.5 kg/m²). At holding pressure, there were no significant differences between females and males in $TI/TTOT$ (0.41 vs. 0.40, $p = 0.653$) or $TTOT$ (4.1 vs. 4.4, $p = 0.210$). When inspiratory flow limitation was induced, duty cycle increased with higher degree of obstruction, but remained similar in males and females at all levels of obstruction. However, female gender was associated with a lower $TTOT$ at all flow-limited conditions ($p < 0.05$ for all comparisons). Subsequently, tidal volumes were lower for females at mild (318 vs. 385cc, $p = 0.02$), moderate (232 vs. 318cc, $p = 0.01$), and severe (169 vs. 208cc, $p = 0.01$) flow-limited conditions as compared to males.

**Conclusion:** Our data demonstrate that the respiratory rate determines the tidal volume during periods of upper airway obstruction. Women have a more brisk response in respiratory rate to experimentally-induced flow limitation. This variable response of respiratory rate may explain differences in the expression of sleep disordered breathing between genders.

**TS 10.05**
**Gender-related differences in CO₂ homeostasis during sleep**

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**TS 10.06**

An Informatics Approach to the Analysis of Sleep Fragmentation in Sleep Related Breathing Disorders

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**Background:** Sleep related breathing disorders often show a high number of awakenings and sleep-wake transitions. Usually sleep fragmentation is quantified in terms of simple statistics such as the number of arousals, of awakenings, and the relative time of wakefulness during sleep related to the time spent in bed (sleep efficiency). Occasionally the sleep stage transitions are also counted but for this statistics there exist no reference values.

**Methods:** In 48 healthy volunteers and 48 age matched sleep apnea subjects we evaluated the duration of sleep stages and wakefulness during sleep. We investigated the distribution of the durations of the individual stages in order to detect underlying statistical properties by applying single and double logarithmic scales.

**Results:** We detected that the distribution of sleep stages follows an exponential distribution. The difference between the sleep stages is just reflected by different time constants. In contrast to this the distribution of wake during sleep follows a power law. This was true for normal subjects and patients with sleep apnea. The patients with sleep apnea had different time constants and different exponents in the power distribution. The difference was such that it favored shorter sleep periods and shorter wake periods in the patients with sleep apnea.

**Conclusion:** This principally different regulation of sleep stages and wakefulness related to the distribution of durations is surprising. We checked this difference also over a variety of species and could still confirm this difference in the underlying laws. We conclude that we found a general law for sleep/wake regulations which can be over a variety of species and could still confirm this difference in the underlying laws. We conclude that we found a general law for sleep/wake regulations which can be

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**TS 11: Sleep In Epilepsy**

**TS 11.01**

Epileptic and non-epileptic hippocampal activity during sleep

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During the assessment of candidates for surgical treatment of temporal lobe epilepsy, chronic hippocampal depth registrations are performed in order to lateralize the primary epileptogenic area.

**Aim:** of this study was to identify both non-epileptic and epileptic interictal activity in different states of wakefulness and sleep. Particularly, we asked whether characteristic patterns are associated with either sleep related or epilepsy related states.

**Methods:** The study included 8 patients who were seizure free after operation based on chronic evaluation by hippocampal depth electrodes. All-night registrations with standard polygraphic derivations were analyzed according to the Rechtschaffen and Kales criteria. Sleep stage (W, S2, S3-4, REM), pathology (epileptic, non-epileptic) and contact coordinate (anterior, posterior) served as independent variables, spectral values as well as frequency and morphology of electrographical patterns as target variables.

**Results:** Differences by frequency analysis: compared to surface EEG, low frequency components are enhanced for waking states within the hippocampus proper. During REM sleep we even found pronounced hippocampal delta activity, whereas for Non-REM differences are not significant. Using pattern analysis, we found that spindling and sleep related sharp waves are generated within the hippocampus, too, yet not synchronously with surface EEG. Epileptic patterns can be distinguished from sleep patterns by intra-burst frequency, sharpness and other qualities.

**Conclusion:** In hippocampal activity influences of both sleep and epilepsy are effective, criteria of differentiation are described.

**TS 11.02**

Corticospinal excitability and intracortical inhibition in NREM sleep of patients with non-lesional focal epilepsy and sleep bound seizures.

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**Background:** In patients with frontal and temporal epilepsy NREM-sleep activates epileptic seizures and facilitates interictal epileptic discharges. Studies using single and paired pulse transcranial magnetic stimulation (TMS) have recently shown that (1) the excitability of the corticospinal motor system is systematically reduced in natural human sleep as compared to wakefulness with significant differences between the sleep stages. (2) intracortical inhibitory mechanisms contribute to these sleep stage related differences.

**Methods:** Using the same TMS paradigms we looked for sleep stage specific changes of corticospinal motor
excitability and the involvement of intracortical inhibitory/facilitatory mechanisms in patients with non-lesional frontal and temporal epilepsies and sleep-bound seizures (n=7). We specifically tested the hypotheses whether corticospinal motor excitability is enhanced and short intracortical inhibition (SICI) is reduced in NREM sleep of epilepsy patients.

**Results:** Corticospinal excitability was similarly reduced in epilepsy patients and in healthy controls as shown by increased motor thresholds and flattening of stimulus-response curves (REM<NREM2<NREM4<wake). In healthy controls SICI and intracortical facilitation (ICF) was significantly enhanced in NREM3/4 as compared to wakefulness and all other sleep stages whereas in NREM2 neither SICI nor ICF differed from wakefulness. In REM sleep SICI was in the same range as in wakefulness, but ICF was entirely absent. By contrast, in epilepsy patients SICI was significantly reduced in NREM-sleep when compared to controls. However, assessment of SICI/ICF was limited to single patients and not feasible during REM-sleep.

**Conclusion:** Impaired intracortical inhibition in NREM sleep may contribute to the pathophysiology of sleep bound seizures in patients with frontal and temporal epilepsy.

**TS 11.03**

**Hypnagogic Paroxysmal Dystonia—Where did it go?**

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Nocturnal or hypnogenic paroxysmal dystonia (HPD) are rarely reported complex motor attacks occurring abruptly during sleep, especially NREM sleep. Most patients show an autosomal dominant inheritance. The clinical semiology is mostly a mixture of dystonia, athetosis and sometimes more rapid flailing movements.

The existence of HPD as a distinct nosological entity has been the cause of much discussion. Many authors consider these nocturnal motor attacks to be frontal lobe epileptic seizures and indeed many patients reported have, in addition to their nocturnal “dystonic” attacks, seizures of obvious epileptic origin or epileptiform activity in the interictal EEG. One of the main points in the debate as to the existence or non-existence of HPD has been the ictal EEG. The lack of ictal changes, apart from a massive desynchronisation, has been used as one of the main arguments for a non-epileptic nature of these attacks. However this argument alone seems not to be valid as the same findings can be seen in surface EEG during frontal lobe epileptic seizures. Conversely in many of the patients presented to support the fact that HPD’s are in fact frontal lobe seizures the dystonia is mostly only a minor part of what is obviously an epileptic seizure and should not be a point of discussion.

There do exist patients who experience pure hypnogenic dystonic episodes that show no other semiology which would relate them to frontal lobe seizures. In the EEG during such episodes the typical delta arousal pattern that is otherwise associated with NREM parasomnias is seen. On complete awakening the semiology (dystonia) abruptly ceases.

We therefore argue that HPD does exist but needs to be re-defined and could, in analogy to confusional arousals, be considered to be an incomplete motor awakening.

Video and EEG findings will be presented to support this hypothesis.

**TS 11.04**

**Seizures with Minor Arrest of Respiration or Tachypnea in Sleep**

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**Introduction:** Epileptic seizures of frontal lobe origin are particularly prone to the effects of sleep. We describe a newly characterized seizure semiology and it’s relevance for polysomnographic investigations.

**Patients and Methods:** A retrospective evaluation was performed of patients examined using Video-EEG-PSG. Respiratory tracings were screened for tachypnea or arrest of respiratory drive associated with epileptiform changes in the EEG. All patients had a diagnosis of epilepsy.

**Results:** An arrest of respiration at the onset of EEG discharges without any other motor activity was observed. EEG changes in these subjects consisted of rhythmic spikes or spike wave series bifrontally with the commencement of the respiratory changes and all were clearly discernable from an EEG arousal. Respiratory changes in patients with supplementary motor seizures (SMA) consisted invariably of tachypnea for the duration of the ictal discharges (rhythmic spikes bifrontally). Although the tachypnea often resulted in a slight increase of SaO2, no desaturations or apneas before the seizures were recorded. A subset of SMA patients exhibited the respiratory changes described above with subtle forms of postural motor seizures, suggesting a continuum of seizure severity, with tachypnea as the only sign on the “subtle” end of the spectrum. Tachypnea, as described above was also seen in patients, with myoclonic/ atonic seizures. These subjects had EEG changes similar to those of the patients with SMA seizures.

**Discussion:** An epileptic seizure is always a clinical event. Conversely, in the absence of clinical signs, discharges in the EEG alone are termed subclinical and are not regarded as seizures. We consider that changes in respiratory frequency or amplitude are “overt signs” of...
epileptic seizures. This is the first description of a subtle seizure type appearing only in sleep and characterized solely by respiratory changes, termed SMARTS = Seizures with Minor Arrest of Respiration or Tachypnea in Sleep.

TS 12: An Overview of the Genetics of Sleep Disorders

TS 12.01
Genetics of Restless Legs Syndrome

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40–60% of the idiopathic RLS patients have a positive family history. So far, no disease causing mutation has been identified. A complex segregation analysis showed evidence for a single major gene acting dominantly with an additional multifactorial component in early age-at-onset RLS families. A possible high phenocopy rate is a major obstacle in the process of identifying causative genes. Three loci for RLS on chromosomes 12q (RLS-1), 14q (RLS-2), and 9p (RLS-3) have been mapped so far. RLS-1 was identified in a French Canadian family, based on a recessive mode of inheritance. In contrast RLS-2 and RLS-3 were identified using an autosomal dominant trait. Performing a genome wide linkage analysis using microsatellite markers we confirmed the region on chromosome 9 (LOD score of 3.78, multipoint analysis) and narrowed the critical region down to 7.5 Mb. In addition, confirmation of RLS-2 was found in a French Canadian family. Genotyping further 12 RLS families for possible linkage to these three candidate regions provide evidence for the likelihood of further genetic locus heterogeneity and the confirmation of RLS-1. Studying MAO polymorphism in the French Canadian population revealed that female RLS patients carrying the alleles of the MAOA gene, which correspond to an elevated MAOA activity, had a greater risk of being affected with RLS than females carrying the low activity alleles. An identification of RLS genes will provide understanding of the molecular mechanisms of RLS and further dopaminergic disorders.

TS 12.02
The genetics of narcolepsy

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Great research was dedicated to genetics of narcolepsy because there is a strong evidence of genetic background of this disease. Familial cases are rare (<10%) but the risk of narcolepsy in a first-degree relative of narcoleptic is 10 to 40 times higher than the general prevalence (0.025%). The most important predisposing allele is DQB1*0602, which is found in up to 95% of narcoleptics. Mutations of the gene encoding the type 2 hypocretin receptor are responsible in a canine model of narcolepsy (autosomal recessive transmission with complete penetrance). Knock-out mice for the precursor ligand for this receptor as well as hypocretin/ataxin 3 transgenic mice present a phenotype similar to human narcolepsy. A mutation in the pre-prohypocretin gene was found in one case of narcolepsy with very young age at onset, very severe symptoms and HLA DQB1*0602 negative. In humans no mutations in the hypocretin receptors 1 and 2 were found. Nevertheless the implication of hypocretin system in human narcolepsy is evident because nearly all sporadic patients have undetectable CSF hypocretin-level.

Linkage study performed in multiple families showed significant linkage at 4p13-q21 and the second study identified in one large French family a susceptibility locus on chromosome 21q. However, none of these results was so far replicated. Twins are usually discordant for narcolepsy and familial cases are frequently HLA DQB1*0602 negative. This and other features show that environmental factors are involved in pathophysiology of narcolepsy.

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TS 12.03
The human circadian system: Living between two clocks

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The circadian clock impacts practically all functions in our body, ranging from activating genes to modifying behaviour and cognitive functions. Although circadian clocks continue to cycle in constant conditions without information about the daily changes of the environment (e.g., light and darkness, warm and cold), it has evolved to optimise the daily sequence of events within a predictably changing world. Thus, understanding how the circadian clock “entrains” to the daily environmental changes is a prerequisite to understand the function of this important biological mechanism. Entrainment of the circadian clock on the individual level is apparent by how the clock embeds itself into the 24-hour-day. In humans, this results in different ‘chronotypes’: some people go to sleep and are active early, others late. The distribution of chronotypes in a population forms a bell shape with the extreme early types (“larks”) at one end and the extreme late types (“owls”) at the other and the majority in between similar to the
distribution of body height, where very short and tall people are a minority, most humans within a given population deviate more or less from the average. Chronotype is partly influenced by genetics, but also by other factors (e.g., light and age). Modern society greatly affects the circadian clock: by predominantly working indoors, we are exposed to much less light than in former times. The 24-hour society, shift work, and frequent travel over many time zones all challenge the daily programme of our bodies. While entrainment evolved to be a harmonic balance between a cyclic environment and the circadian clock, most of us now live between rather than with the external and the internal clocks challenging health and quality of life. A detailed understanding of the circadian clock and its entrainment is a prerequisite to counteract these difficulties.

TS 12.04
Genetics of Obstructive Sleep Apnea

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Obstructive sleep apnea is the most common disorder of respiratory control, present in some 2–5% of the population and producing neurocognitive and cardiovascular morbidity. This state-dependent condition has a clear genetic component, with a substantially increased risk for snoring and sleep apnea among relatives of affected individuals. Almost a third of the variance in the severity of sleep apnea in a US population is explained by familial clustering. The pathways by which inheritance could predispose to sleep apnea include anatomic features of the obese condition and of craniofacial form; however, current data suggest that these heritable traits explain only a half of familial cases. The factors related to respiratory control, namely the control of ventilation and the impact of sleep on ventilatory drive, act and interact to produce repetitive events during sleep, which in turn influence the pathogenesis of illness. Preclinical models suggest genetic risk influences features of dynamic control including the response to changes in chemosensory drive and the response to re-oxygenation, including the appearance of unstable breathing. Thus research has begun to identify causative factors that might pre-dispose or modulate the physiology of sleep apnea, and provide insight into pathways that could increase (or decrease) the risk of progression to illness or that might be modified to reduce apnea expression.

Support: Veterans Affairs Research Service and NIH

TS 13: Recent advances in the treatment of insomnia

TS 13.01
Sleep duration and insomnia and their relevance for depression, obesity and mortality

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In recent years several epidemiological studies have dealt with the question whether short or long sleep times are coupled with increased mortality. Surprisingly, it was shown that especially longer sleep durations (>8 hours) predicted increased mortality. On the other hand some studies indicated that short sleep times and symptoms of insomnia were related to increases in body mass index, thus stimulating the hypothesis that short sleep leads to obesity. Recent epidemiological data from the US and Japan in large samples strongly support the hypothesis that contrary to expectation not very short sleeping times, but sleeping times longer than 8/9 hours are coupled with increased mortality in longitudinal studies. The reason for this relationship still is unclear, but it may be hypothesized that subjects suffering from undetected sleep apnea may be at the core of this relationship, if the apnea is not treated. With respect to the relationship between obesity and short sleep times/insomnia, several studies have been published looking at the issue for example in patients who develop diabetes. It has been shown that subjects with shorter sleeping times are more prone to develop diabetes in the long run than those with normal sleep times. In an own study we investigated nocturnal leptin excretion, which is thought to be one of the driving forces between weight gain in insomniac patients. In our study in a relatively small sample of 11 patients with primary insomnia, no increase or decrease of this hormone was shown, thus contradicting the assumption that short sleep or disordered sleep leads to a decrease of this hormone. With respect to relationships between insomnia and depression the picture seems rather clear. Up to now at least five epidemiological longitudinal studies have demonstrated that insomnia at a given point in time is predictive of the development of later depression. These data strongly support the notion that early and aggressive treatment of insomnia might be considered as a preventive approach for psychiatric sequelae of insomnia.
Brief use of zolpidem in a 6-week CBT treatment for insomnia

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Manualised CBT for insomnia delivered by nurse practitioners: results from studies conducted in primary care and in oncology

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Aims: To summarise outcome data from three recent randomised clinical trials of CBT for insomnia, where nurse practitioners delivered the interventions

Methods: Across three trials, two community-based and one based in oncology outpatient settings (secondary insomnia), a total of 490 adults with persistent insomnia were randomised either to CBT or treatment as usual (TAU). Health Visitors and Cancer Nurse Specialists were trained and supervised in the delivery of a validated, manualised therapy provided in small group format—the ‘Glasgow Model’.

Results: CBT was associated with an average reduction in sleep-onset latency plus wake time after sleep onset of approximately 60 minutes per night of sleep, relative to little change in TAU. Demographic and clinical factors did not contraindicate response to this form of insomnia treatment.

Conclusions: Clinical psychologists/behavioural sleep medicine specialists have more to offer than direct clinical work. Insomnia assessment and treatment programme development, including the training and supervision of first-level CBT practitioners, offers one possible way forward.

Combined CBT plus Medication in the Treatment of Insomnia: Rationale, Indications, and Preliminary Outcomes


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Background: The use of cognitive-behavior therapy (CBT) and medication in combination for treating insomnia has received limited research attention. Theoretically, combined approaches should optimize outcome by capitalizing on the more rapid effects of medication and the more durable benefits of CBT. The available evidence, however, is unclear as to whether a combined intervention has an additive effect on outcome. This paper presents preliminary data from an ongoing clinical trial evaluating the efficacy of CBT, alone and combined with medication (zolpidem), for the treatment of persistent insomnia.

Methods: The objectives of the study were to evaluate the short-term effects of CBT, alone and combined with medication, and compare the efficacy of different maintenance strategies to optimize long-term outcomes. Thus far, 143 adults (60% women; mean age of 50.3 years) with primary insomnia have completed the acute treatment phase (6 weeks) and 107 have completed the extended treatment phase (6 months). Patients treated with CBT alone initially were randomized to extended CBT or no 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).

Results: Preliminary analyses indicate that CBT is equally effective when used alone or combined with medication during the initial phase of therapy, with sleep efficiency reaching 88% in both conditions. However, there is a slight advantage for the combined approach to produce a greater increase in total sleep time. Results from the extended phase of therapy suggest that the addition of maintenance CBT promotes long-term maintenance of sleep improvements.

Conclusions: Based on these preliminary findings, we will discuss the rationale and clinical indications for combining CBT and medication and examine optimal models for combined and maintenance therapies in the management of insomnia.

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TS 14: Metabolic Complications of Sleep Disorders

TS 14.01
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TS 14.02
Metabolic effects of sleep deprivation
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TS 14.03
Systemic inflammation in sleep disordered breathing
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TS 14.04
Sleep Apnea and Dysregulation of Lipid Metabolism
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Obstructive Sleep Apnea (SA) is characterized by recurrent upper airway obstructions during sleep leading to intermittent hypoxia (IH) and sleep fragmentation. SA is an independent risk factor for cardiovascular diseases and is associated with increased incidence of myocardial infarction, stroke, and death. SA is associated with insulin resistance, hypercholesterolemia and progression of atherosclerosis. There is recent evidence that SA is associated with fatty liver disease, independent of obesity. We have previously shown that IH leads to progression of insulin resistance and glucose intolerance in obese mice. We have now examined the effects of experimentally-induced intermittent hypoxia (IH) on serum lipid levels, liver lipid content and pathways of lipid metabolism in the absence of obesity. Lean C57Bl/6J mice were exposed to IH for five days. Exposure to IH increased serum levels of total cholesterol, LDL and HDL cholesterol, and phospholipids, as well as liver triglyceride content. IH increased sterol regulatory element binding protein 1 (SREBP-1) levels in the liver and up-regulated stearoyl-CoA desaturase 1, an important gene of triglyceride and phospholipid biosynthesis controlled by SREBP-1. In addition, IH up-regulated pathways of lipoprotein secretion, including microsomal triglyceride transfer protein and apolipoprotein B, and decreased protein levels of scavenger receptor B1, which regulates uptake of cholesterol esters and HDL by the liver. We conclude that exposure to IH for five days (1) increases liver triglyceride content due to up-regulation of lipid biosynthesis; (2) increases serum cholesterol and phospholipid levels due to up-regulation of lipoprotein secretion and down-regulation of cholesterol uptake in the liver. We hypothesize that IH of SA may lead to hypercholesterolemia and fatty liver disease.

TS 14.05
Sympathetic activation in sleep apnea
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TS 15: Daytime consequences of restless legs syndrome

TS 15.01
Symptoms of attention-deficit/hyperactivity disorder in adults with restless legs syndrome
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Restless Legs Syndrome (RLS) and Periodic Limb Movements of Sleep (PLMS) have been associated with decreased quality of life, as well as an increased risk of heart disease, hypertension, diabetes, and psychological conditions. This may be due to impaired physiologic functions when sleep is disrupted. Adult patients with RLS have an increased risk of symptoms related to attention-deficit hyperactivity disorder (ADHD). Children with ADHD have a higher risk of PLMS, a good marker of RLS in children, than control children. The parents of the ADHD children also have a greater risk of RLS than control parents. A cross-sectional survey of 866 children found a positive association between symptoms of inattention, hyperactivity, RLS, and PLMS. Genetic studies indicate that there may be abnormalities in the dopamine transporter and D4 dopamine receptor in patients with ADHD. A gene for RLS has not been identified. PET scan studies indicate that ADHD and RLS are both characterized by a deficiency of dopamine and symptoms respond to medications that increase dopamine concentrations. Both conditions are associated with low ferritin concentrations, and low iron concentrations result in abnormal dopamine activity. ADHD and RLS symptoms may improve with iron therapy.
RLS is difficult to diagnose in children and symptoms may be misinterpreted as ADHD. Children being evaluated for ADHD symptoms should be asked about sleep problems and growing pains as they may have undiagnosed, comorbid RLS. There are numerous conditions, such as depression or bipolar, anxiety, seizure, or conduct disorders, that may mimic ADHD symptoms. Patients with either ADHD or RLS may have a greater risk of comorbid depression or anxiety. The management of ADHD symptoms in patients with RLS is not well studied. Patients may benefit from nonpharmacological therapies alone. These treatments include behavioral therapy, cognitive therapy, and school/workplace modifications. Pharmacologic therapies for ADHD include stimulants, antidepressants, and alpha-adrenergic agonists. Stimulants, first line treatment for ADHD, may improve symptoms of fatigue in patients with RLS. Clonidine may be helpful in those with comorbid hypertension and RLS. Open-label studies suggest that dopamine agonists may improve both ADHD and RLS symptoms. Antidepressants may aggravate RLS and PLMS.


TS 15.02
Cognitive functions in RLS patients with PLM and in PLMD patients without RLS

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Deficits in daytime performance due to sleep loss are an universal experience. Several studies showed that sleep deprivation may have a negative impact on mood, cognitive performance, and motor function. Specific neurocognitive domains, such as executive function, seems to be particularly vulnerable to sleep loss. However, few studies in humans demonstrate that neural systems involved in executive function (i.e., prefrontal cortex) are more susceptible to sleep deprivation in some individuals than others. Sleep deprivation associated with disease-related sleep fragmentation, such as sleep apnea and restless legs syndrome (RLS), also results in neurocognitive deficit similar to those observed in sleep restriction/sleep loss studies (1). There are several published data on cognitive function in sleep apnea, but data on RLS are very few and usually not related to the objective polysomnographic results. Moreover, it has been recently reported that RLS patients are at increased risk of having specific anxiety and depressive disorders and that a considerable proportion of the excess morbidity for depression and panic disorder might be due to RLS symptomatology (2). These psychiatric disorders could contribute to the neurocognitive deficit. We studied 10 patients with idiopathic RLS and PLM (mean age = 49 yrs; mean PLM index = 37.8), 10 patients with PLMD and without RLS (mean age = 52 yrs; mean PLM index = 39), 10 patients with psychophysiological insomnia (mean age 50 yrs; mean PLM index = 4.8) and 20 age-matched controls. A cognitive impairment has been found in the three patient groups in comparison to controls on: reaction time test (sustained attention), Corsi supraspan test (learning test), digit span forward (verbal short-memory). The lowest scores have been found in the RLS group; in the same group, significantly lower scores in comparison to the others have been found in the Purdue Pegboard test (motor and constructional abilities). Concerning the polysomnographic data, RLS group showed a significantly reduced sleep efficiency, but no difference was observed in the sleep percentages of NREM and REM stages, as well as in the number of arousals/hour of sleep, among the 3 patient groups. The results of Epworth Sleepiness Scale were similar in patients compared to controls, as well as those obtained in the Beck Depression rating scale.

Our data suggest that RLS “per se” may determine a cognitive impairment and, moreover, may worsen the negative profile caused by PLM-sleep fragmentation. The cognitive deficit in RLS patients is unrelated to excessive daytime sleepiness or depressive symptoms. Further studies evaluating the specific treatment for RLS may clarify the possible reversibility of the cognitive impairment.


TS 15.03
EEG-mapping and psychometric investigations in RLS patients compared with normal controls

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Aims: While sleep disturbances due to RLS have been studied quite well polysomnographically, little is known on the electrophysiological function during daytime. Daytime electrophysiological dysfunction may be associated with noopsychic and thymopsychic deficits, which however, may also be due to the sleep disorder. The aim of the present study was to investigate the diurnal EEG of drug-free RLS patients compared with normal controls by EEG-mapping. Clinical symptomatology was evaluated by rating scales, noopsychic and thymopsychic were measured by psychometric tests.
Methods: Investigations comprised brain mapping of the vigilance-controlled EEG and the Zung self-rating scales for depression and anxiety, the Quality of Life Index, the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale for evaluation of clinical symptomatology. Mental performance (noopsych) was investigated by the following tests: Lehr’s Mehrfachwahl-Wortschatz-Test, a measure of crystallized (verbal) intelligence; the Benton Test for the evaluation of visual memory (correct reproductions and errors); Grünberger Verbal Memory Test for general, associative and numerical memory; Grünberger Fine Motor Test for the assessment of psychomotor activity. Thymopsychic evaluation included: drive, mood, affectivity, and wakefulness by 100 mm visual analogue scales (VAS), the Von Zerssen Mood Scale and the Spielberger State/Trait Anxiety Inventory. Psychometric investigations were carried out during mid-morning hours.

Results: Statistical analysis demonstrated an increase in absolute delta and absolute and relative alpha-2 power, a decrease in absolute and relative alpha-1 power, an acceleration of the dominant frequency and the alpha centroid and a slowing of the delta/theta centroid, as well as a non-significant attenuation in total power. These findings are characteristic of dissociated vigilance changes described in depression. Indeed RLS patients demonstrated significantly higher depression and anxiety scores, lower quality of life and deteriorated sleep quality. The score of the Epworth Sleepiness Scale was not elevated, which is quite in contrast to the increased daytime sleepiness observed in other highly prevalent organic sleep disorders (e.g. sleep apnea). Psychometric investigations demonstrated normal crystallized intelligence and quantitative but not qualitative aspects of visual memory. In the noopsych, total verbal memory was significantly reduced, while general, associative and numerical memory as well as psychomotor activity tended to be reduced. In the thymopsych, drive, affectivity, wakefulness and well-being were significantly deteriorated in RLS patients as compared with normal controls.

Conclusions: Daytime EEG mapping revealed neurophysiological correlates of depression in RLS, which was confirmed by self-ratings at the symptomatological level. RLS patients also exhibited a deterioration in the thymopsych and noopsych, measured by psychometry.

TS 16: Restless Legs Around the World

TS 16.01
Research Activity in Restless Legs Syndrome in Europe

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Over the last years, an increasing number of researchers from different European countries coming have focussed their interest in research on Restless Legs Syndrome. As a result, a European section has been created within the International Restless Legs Syndrome, with yearly meetings in Munich during which results of ongoing research is shown and new common projects are discussed.

At present, several projects are ongoing or about to be completed:

- Creation of a common database of patients
- Genetics: Under the coordination of J. Winkelmann (Max-Planck-Institute, Germany), a numerous group of investigators belonging to the European RLS group are performing a sib-pair analysis of patients with familial RLS, with the intention to confirm published disease loci and also support the identification of disease causing genes. Sib pair analysis is a form of non-parametric linkage analysis in which markers are tested for linkage to a disease (or phenotypic trait) by measuring the extent of which affected sib pairs share marker haplotypes. Originally this approach has been used to identify disease genes in complex disorders where several genetic as well as environmental factors contribute to the disease phenotype.

TS 15.04
Quality of Life, Mood, and Cognition in RLS patients

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Most studies have focused on the sensory and motor components of restless legs syndrome (RLS) during the evening or night. Daytime consequences of RLS have received only little attention so far. However, there is emerging evidence that this frequent sleep disorder is also associated with impaired daytime functioning. In an ongoing project we are currently exploring quality of life, mood, and cognition in patients with RLS. A first study explores whether patients with RLS differ from a control group matched for age, gender and education on measures of attention, memory, and executive functions. Neuropsychological measures were chosen to provide adequate norms and to enable comparison of performance of RLS patients both to norms and the control group. A second study investigates cognitive performance in patients with and without RLS. All patients of this study were screened for dementia with the Mini-Mental-Status-Examination. Uremic patients with untreated RLS, with augmentation during treatment of RLS and patients with no RLS were assessed with a measure of verbal fluency and the tower of Hanoi. Our analyses will focus on group differences between subjects with and without RLS and on the influence of disturbed sleep or disturbed mood on cognitive performance in these subjects.
New instruments for measurements for long-term efficacy of therapeutic agents. Within this project, a new rating scale to measure augmentation has been developed within the European RLS group. The group has also finalized a multicentric study on long-term treatment with levodopa, and has recently finished the validation of the augmentation severity rating scale (ASRS).

In addition, several large scale epidemiological studies have been performed over the last years trying to further characterize the population at risk and the burden of disease for those affected. Furthermore, Europe has been subject to several large scale therapeutic trials over the last decade, during which new molecules and therapeutic concepts are being developed.

Taken together, the European RLS group is an example of a spontaneously emerged platform that has helped to converge the creative ideas of small scale groups into multicentric, large scale studies across the continent combining the expertise of specific research groups with large scale recruitment capabilities.

TS 16.02
Restless Legs in North America. Birth of the Restless Legs Syndrome Foundation and the International RLS Study Group

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In the early 1990’s the U.S. was the birth place of two new organizations important for the development of scientific and medical research, patient support, and Restless Legs Syndrome (RLS) awareness around the world—the Restless Legs Syndrome Foundation (RLSF) and the International Restless Legs Syndrome Study Group (IRLSSG).

The RLSF has a full time staff, a patient sponsored board which appropriately has the ultimate say in policy, a medical advisory board which insures accuracy of RLSF materials distributed to patients, physicians and the media as well as a scientific advisory board which reviews grant requests for possible funding. The stated goals of the RLSF are to provide support for the organization of and distribution of materials to over 70 local RLS support groups across the USA, to increase the awareness and understanding of RLS amongst patients, physicians and the media and to provide financial support for research into the causes and treatment of RLS and Periodic Limb Movements in Sleep (PLMS). The medical advisory board has become much more internationally representative with members from Germany, Spain and Italy added in the past few years. The RLSF recently organized a meeting of similar RLS based support group organizations from other countries with the purpose in mind of coordinating efforts amongst these organizations in order to create increased awareness of RLS and PLMS all around the world. This is important since many of these organizations are nascent in their nature and have not had the organizational experience of the RLSF, nor do many of them have the financial resources to do more expensive projects without some international support from other organizations including the RLSF.

The IRLSSG is comprised at last count of 143 physicians and scientists from around the world dedicated to collaborative research on RLS and PLMS. The first major project of the IRLSSG was to come up with a joint position as to what comprised the essential versus the non-essential or ancillary features of RLS. The joint definition of RLS was first published in the journal Movement Disorders 10 years ago and these criteria were re-worded for greater clarity and re-published by the IRLSSG in conjunction with an NIH consensus conference in the journal Sleep Medicine in 2003. The next important project was to come up with a rating scale for the severity of the symptoms of RLS. This was important since objective measures such as polysomnography do not measure the essential but only the ancillary features of RLS. It also became apparent that major pharmaceutical companies would not and could not do expensive and time consuming polysomnographic studies in the numbers required for approval of their products by regulatory agencies such as the FDA. After many drafts and input from many members of the IRLSSG, the rating scale was finalized and submitted to a world-wide validation analysis involving many centers and many patients. The scale has turned out to be a reliable and valid instrument for the measurement of the symptoms of RLS, albeit with a high placebo effect. The scale, now called the IRLS, has been used as the principal endpoint for most of the major studies conducted by industry for the approval of their drugs for the treatment of RLS. The IRLSSG is now also actively involved in the establishment of a scale to measure RLS augmentation, a project to determine potentially new rules for scoring PLMS based upon a mathematical analysis of the regularity of occurrence of certain PLMS patterns and a multi-center collaborative genetics project under the auspices of the European subsection of the IRLSSG.

TS 16.03
Restless Legs in Latin-America

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In South America, and specifically in Chile, only in recent years is possible to see clinical interest regarding RLS. We are aware of only 2 studies of prevalence of this
disorder in Latin America; a study dated in year 2000 which suggests a 13% of prevalence in Chilean adult population and a recent study of Brazilian patients on hemodialysis which found a prevalence of 14%. Most cases on Chile remain underdiagnosed for years (even 60 years in some cases) before a correct diagnosis is done, we have seen a low awareness of RLS even in neurologists and using inappropriate medications. Secondary causes are fairly common as well. We found a prevalence of 26% in uremic patients undergoing dialysis in accordance with other authors, most them were not diagnosed before studied and after the correct diagnosis an effective treatment allow them to keep in dialysis. An open trial with pramipexole done by our group showed clinical efficacy with low side effects in this severely impaired group of patients. During this year by the first time we organized a meeting entirely dedicated to RLS in our country, with the aim to increase clinical awareness of the importance of a correct diagnosis, the great impact of RLS on patients’ quality of life and we could heard live reports from severely affected patients and hereditary cases covering many generations.

TS 16.04
Restless Leg Syndrome (RLS) in Thailand: RLS, ADHD, and iron deficiency—overlapping disorders

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The objective of this study is to determine the prevalence of restless legs syndrome (RLS), periodic limb movement in sleep (PLMS), and attention deficit hyperactivity disorder (ADHD) in a population of children suffering from iron deficiency. In recent surveys by Thailand National Institute for Child and Family Development between 1996–1999 school-age children under 18 years in sub-urban areas, we found between 13–14% with iron deficiency, 10–15% with PLMS, and 5–10% percentage with ADHD. We further investigated this population using studies of ferritin level to assess iron deficiency, activity meter recording to establish the PLMS, and questionnaire screens for symptoms of ADHD and RLS. 400 children under 18 years old in 6 suburban villages in Thailand who are within the field-study area of Mahidol University center at Salaya were screened for low ferritin (<50 microgram/liter). 50 children with low ferritin were selected and compared to 50 children with normal ferritin matched for age and sex. Three night recordings of leg movements were performed using a portable meter and associated software to calculate the activity overnight as well as the number of PLM broken down into hourly units. All children were screened for ADHD with the Connors scale. The Hopkins diagnostic interview was administered to the children and/or their parents to determine the presence of the restless legs syndrome. Childhood RLS was determined by a) the presence of PLMS and either b) a family history of RLS or c) a positive RLS diagnosis using the Hopkins interview. First, we found that children with iron deficiency have a higher prevalence of RLS, ADHD, and elevated PLMS at night. Approximately half of the children with iron deficiency have either ADHD or PLMS compared to less than 10% of the control children. Second, we found that children with both iron deficiency and ADHD also have a still higher prevalence of symptoms of RLS and PLMS. The majority of these children have PLMS and that some also have symptoms of RLS. The study also indicates that RLS and PLMS are a significant population in Oriental as well as Western populations, and RLS, ADHD, and iron deficiency may be overlapping disorders.

TS 17: Sleep in mental retardation

TS 17.01
Why is it important to study sleep of people with intellectual disabilities

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Aims: An actual problem in intellectual disability medicine is that people with difficult-to-treat seizures and/or behavioural problems often have sleep difficulties such as fragmented sleep. Based on this observation we did sleep recordings and clinical examinations to such patients.

Methods: Clinical examination, polysomnography and multiple sleep latency test were performed to 37 consecutive patients in the year 2004. There were 24 males and 13 females. Their age ranged from 6 to 64 years, the mean age ± standard deviation being 28.0±30.3 years. Down syndrome was the most common underlying disorder (9/37 or 24%). The other syndromes and genetic abnormalities included fragile-X, Angelman, Wolf-Hirschhorn, Pallister-Killian, Prader-Willi and Rubinstein-Taybi syndromes, aspartylglucosaminuria and other conditions.

Results: Altogether 24 out of 37 patients or 65% had a definite sleep disorder. Sleep apnea was diagnosed in 15 patients (41%), seven of them had Down syndrome. Restless legs syndrome and/or periodic limb movement disorder in sleep was found in seven patients (19%), while two patients had marked hypersomnia without sleep apnea.
Sleep disturbances are common in children with intellectual disabilities, and several neurophysiological studies have been performed in the past in order to find specific polysomnographic phenotypes. Although we could find sleep macrostructural alterations that are in most cases aspecific (such as REM and/or slow wave sleep reduction) no attempt have been made to modify criteria for scoring in order to adapt to the specific patterns of each syndrome. Also, no data are available on sleep microstructure in these subjects. We analyzed the sleep architecture and sleep microstructure by means of sleep cyclic alternating pattern in some forms of genetic mental retardation and mainly Angelman syndrome, fragile X syndrome and autistic syndromes. We performed a polysomnographic recording (EEG, EOG, EMG) after one adaptation night in 16 autistic males aged 6–12 years, compared with that of 12 normal controls. Sleep macrostructure showed only a reduced sleep period time, compared to normal controls while sleep microstructure showed a decrease in CAP rate and in CAP time during slow wave sleep together with a reduction in the total number of A phases, compared to normal controls. These results suggest an alteration of arousal mechanisms in autistic children (lower level of arousability). We also analyzed sleep in Angelman syndrome (AS) that have specific awake and sleep EEG patterns. The presence of the characteristic high-amplitude potentials of AS throughout the entire recording and the reduced occurrence of K complexes, sleep spindles and rapid eye movements, caused some difficulties in scoring sleep by means of criteria arranged for normal subjects; and therefore we modified sleep scoring criteria for each stage. The presence of typical EEG patterns such as the 2–3 c/s bursts activity makes difficult scoring sleep macrostructure that showed a significant reduction in sleep efficiency, and in the percentage and duration of REM sleep while the percentage of SWS was significantly higher. Further, we also analyzed sleep in Angelman syndrome comparing with normal and autistic subjects. X-fragile subjects showed a significant reduction in sleep efficiency, and in the percentage and duration of REM sleep while the percentage of SWS was significantly higher. Further, we also analyzed sleep in Angelman syndrome comparing with normal and autistic subjects. X-fragile subjects showed a significant reduction in REM percentage, with a reduced length of sleep compared to normal controls, but not compared to autistic group, without particular differences in NREM sleep. CAP analysis, however, showed a significant reduction in CAP rate and in A1 percentage. These results demonstrated that the CAP analysis could be able to discover relevant differences not disclosed by sleep macrostructure analysis between two mental disabilities disorders. From these studies we can argue the need for specific sleep researches in genetically determined mental retardation, especially in those syndromes in which a specific EEG patterns is present, to avoid that “non specific” sleep alterations continue to be described in these syndromes.
TS 17.04
Sleep apnea in patients with mental retardation
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Sleep apnea is a public health concern in general adult population. The prevalence of sleep apnea among men is 2–8%. Among women the prevalence is 1–2% before menopause and 3–4% after menopause. In morbidly obese subjects the prevalence may be higher than 70%. Obesity is common among mentally retarded. In many mentally disabled subjects the cranio-facial structure and buccopharyngeal anatomy are abnormal with narrow upper airways. The prevalence of sleep apnea is very common for example in Pierre Robin syndrome (67–86%), Fragile X (50–60%), Trisomia 21 (30–65%), Prader-Willi (over 30%) and Rubinstein-Taybi (over 50%). Surgery is indicated in case of hypertrophy of the adenoids and tonsils. Also nasal obstruction should be treated. We have started to treat Down patients with radio-frequency thermo-ablation. In most cases nasal CPAP is the treatment of choice. Often mentally retarded can learn/habituate to use the mask with excellent results. However, starting CPAP demands a lot of patience. Usually our mentally retarded patients spend two days in our sleep clinic. During this time they and their care-givers are taught to use CPAP. If sleepiness has persisted in spite of treatment, modafinil has been started. Some of the benefits of treating OSAS in mentally retarded are: better quality of life, less behavioral problems, easier to live at home, no need for institutional care, higher vigilance, prevention of metabolic and CVD diseases. Treatment of OSAS is cost-effective and intellectually disabled subjects with suspected sleep apnea should be properly investigated and treated.

References

TS 18: Sleep Related Eating Disorders (SRED)

TS 18.01
Sleep-Related Eating Disorder: Clinical Features, Treatment, and Differential Diagnosis
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The Sleep-related eating disorder (SRED) was first described in the early 1990s, and is characterized by arousals after sleep onset associated with compulsory nocturnal eating behaviors. There are varying degrees of conscious awareness during the eating episode, and inconsistent recall for the event following awakening the next morning. SRED is undoubtedly a heterogeneous syndrome. It may be primary, or may be associated with other sleep disorders such as restless legs syndrome, periodic limb movements of sleep, sleep-disordered breathing, or disorders of arousal (confusional arousals, sleepwalking, or sleep terrors). The prevalence of SRED (occurring at least once weekly) may be

Aims: To assess the effect of behavioural intervention (BI) for sleeplessness in children with autism spectrum disorders (ASD) on the children’s sleep and daytime behaviour and their mothers’ mental health.

Methods: The parents of 36 children with an ASD aged between 3 and 16 years (34 males, mean age 8.3 years, sd 4.1) took part in a randomised controlled trial with a wait-list control group. BI was discussed in one therapist session and supported by weekly telephone contact for 6 weeks. Pre- and post-treatment a composite sleep disturbance score (CSDS) was derived from parent-completed sleep diaries, actigraphs were worn by the children for at least 5 nights and parents completed the Developmental Behaviour Checklist to assess child behaviour and the General Health Questionnaire to measure their own mental state.

Results: CSDSs were significantly reduced to sub-clinical levels by the treatment (p<0.001) although there were no significant changes in the children’s objective sleep patterns. Treatment was associated with widespread improvements in reported child behaviour but effects on maternal mental health were limited to reduced anxiety.

Conclusions: BI of sleeplessness may have benefits for children with ASD and their mothers but the mechanism underlying the change is not improved objective child sleep. Questions remain about whether the children’s objective sleep disturbance requires treatment and how this might be achieved.

References
as high as 5%. There is a female predominance, and a variable association with diurnal eating disorders such as anorexia or bulimia nervosa. SRED is likely synonymous with the nocturnal eating syndrome (NES) which according to the International Classification of Sleep Disorders is defined as recurrent awakenings from sleep associated with an inability to resume sleep without eating or drinking. SRED is to be distinguished from the night-eating syndrome as described by Stunkard. That disorder is characterized by…. High caloric foods are eaten with preference (chocolate, sweets, pasta, peanut butter, or milkshakes). Fruits and vegetables are ignored. Alcohol is rarely ingested, even in those who drink alcohol socially or who have abused alcohol in the past. SRED has been associated with a number of medications. Zolpidem appears to be a prominent offending agent. Adverse consequences of SRED include: (1) eating peculiar forms or combinations of food, (2) insomnia related to sleep interruption, (3) sleep-related injury (cuts, burns, poisoning), (4) dangerous behaviors performed while seeking food, (5) morning anorexia, (6) adverse health effects (weight gain, diabetes, consuming allergic foods). Due to the possibility of an underlying sleep disorder, evaluation of SRED must include full video-PG monitoring and interpretation by an experienced sleep medicine clinician. Food should be available at the bedside. The treatment of SRED is directed first at controlling any underlying sleep disorder. The combination of carbidopa/L-dopa with an opiate at bedtime may be effective. Topiramate at bedtime is a promising new treatment. Cognitive-behavioral therapies and hypnosis are usually not effective.

(II) Sleep-Related Eating Disorder (SRED)
Clinical Findings
The first report on abnormal nocturnal eating that utilized PSG monitoring was by Whyte and Kavey in 1990, which called attention to “somnambulistic eating” in 3 patients. Although SW remains the most commonly identified predisposing condition for SRED, other conditions and precipitating factors have been identified, such that in 1991 our center reported on “sleep-related eating disorders” in 19 patients, with a subsequent report in 1993 on a total of 38 patients. The following comments were made by our index patient: “I have buttered pop cans and then tried to eat them… I will take the big container of salt—not the salt shaker—and I’ll pour it in my hand and I’ll eat it just like that. Why do I eat salt sandwiches? That’s a biggie… I have sat at the kitchen table eating pancakes at two o’clock in the morning with no clothes on… How primitive can one get? Leftover casseroles—it’s awful.” The hallmark of SRED is involuntary eating and drinking during sleep that usually occurs during partial arousals from sleep, with limited or no recall the next morning. However, a broad range of consciousness and of subsequent recall can be present. Problems associated with recurrent episodes of SRED include the sloppy consumption of peculiar forms or odd combinations of food, or of inedible or toxic substances; insomnia from sleep disruption; sleep-related injury; morning anorexia (lack of hunger) and abdominal distention; and adverse health consequences (e.g. weight gain/obesity). Most affected people report a nightly frequency of eating, including multiple times nightly. The episodes of eating can occur during any time of the night. High caloric foods are eaten with preference, such as chocolate, sweets, pasta, peanut butter, and milkshakes; fruits and vegetables are ignored. Alcohol is rarely consumed at night, even in those who enjoy drinking alcohol or in former alcoholics. There is typically a lack of hunger or thirst during episodes of SRED. If an individual is interfered with during an episode, then the usual response is irritability and agitation. Simple foods or entire hot or cold meals can be prepared, even cooked, and then consumed. Food is often brought back to bed, often to the consternation of the bed partner. A preliminary study utilizing a self-report questionnaire found a nearly 5% prevalence of SRED, defined as eating during partial awakenings from sleep at least once weekly. This included a prevalence of 4.6% in an unselected university student group. This study suggests that SRED may be a common and considerably under-recognized problem. SRED is a female-predominant, with approximately two-thirds to three-quarters of published cases being female. The age of onset is usually in the late teens or early twenties, but a very broad range exists. The onset can be insidious and sporadic, or it can be precipitous and fulminant with rapid development of nightly episodes of eating. SRED is often a relentless, longstanding disorder. Although it can be an idiopathic disorder, it often is associated with a primary, underlying sleep disorder or other clinical condition. For example, SW is the most commonly associated sleep disorder, although once eating becomes part of the behavioral repertoire of SW, it quickly becomes the predominant, if not the exclusive SW behavior. Other sleep disorders that can be closely associated with SRED include restless legs syndrome (RLS), obstructive sleep apnea, and circadian rhythm disorders (such as irregular sleep/wake pattern). Medication-induced (amnestic) SRED has been reported with zolpidem and sporadically with other psychotropic agents. Onset of SRED can also occur with cessation of cigarette smoking, cessation of alcohol and substance abuse (especially cocaine and amphetamine), acute stress (usually involving major separation reactions), after daytime dieting, and with onset of narcolepsy, migraine headaches, and other conditions. SRED at times can be associated with daytime eating disorders (such as bulimia nervosa), and with a nocturnal dissociative disorder (e.g. multiple personality disorder, with one of the “alter” personalities being a nocturnal eater). Serious complications can occur on account of recurrent nocturnal eating:
(1) Eating peculiar forms or combinations of food (e.g. frozen pizzas; raw bacon; peanut butter, salt and sugar sandwiches; cat food sandwiches), or inedible or toxic substances (e.g. cigarettes, coffee grounds, glue, nail polish; ammonia-containing cleaning compounds) can be hazardous. (2) Insomnia related to sleep disruption from repeated
episodes of eating, with daytime sleep-deprivation symptoms: tiredness, fatigue, irritability, moodiness, interpersonal problems, reduced attention span, diminished memory, and sub-par work or school performance. (3) Sleep-related injury: cutting oneself from carelessly cutting food or opening cans, etc; internal or external burns from consuming or spilling hot or scalding foods or beverages; poisoning and internal injuries from ingesting toxic substances. (4) Dangerous behaviors performed while seeking food: e.g. driving a car while half-asleep, or starting a fire in the kitchen while engaged in sleep-related cooking prior to eating. (5) Morning anorexia, often with bloating and no desire to eat breakfast. (6) Adverse health consequences from recurrent binge-eating excessive quantities of high-caloric foods; excessive weight gain/obesity; destabilization (or precipitation) of diabetes mellitus (type II; type I), hypertriglyceridemia, hypercholesterolemia; consuming foods to which is allergic; consuming foods that are contraindicated in patients receiving monoamine oxidase therapy; overnight fasting prior to next-day surgery can be compromised; etc. Secondary depressive disorders may emerge from longstanding personal dejection and a sense of failure over the inability to control the nocturnal eating.

Differential Diagnosis

There are two main differential diagnostic considerations for abnormal nocturnal eating, besides SRED: (1) Nocturnal Bulimia Nervosa or Binge-eating Disorder (i.e. extensions of a daytime Eating Disorder) (2) Nocturnal Eating Syndrome.38 If inappropriate compensatory behavior in order to prevent weight gain from the nocturnal eating is present, such as self-induced vomiting, enemas, misuse of laxatives, diuretics or other medications, or if there is body image distortion, then an Eating Disorder should be diagnosed (bulimia nervosa, binge-eating disorder, anorexia nervosa). However, patients with longstanding SRED and excessive weight gain may eventually fast during the daytime and/or engage in excessive exercise to prevent further weight gain and obesity. If a history of excessive eating between the dinner and sleep onset is present, then the diagnosis would probably be a different eating disorder called “Nocturnal (Night) Eating Syndrome,”38 which is not a Parasomnia, but rather a disorder of wakefulness. Sometimes patients with SRED will eat dinner, or have a substantial second dinner shortly before going to bed at night in futile attempts to suppress the compulsion to eat after subsequently arousing from sleep.

Treatment of SRED

Treatment is at first directed at controlling any underlying sleep disorder, or to discontinue any medication that is suspected to be causing or promoting the SRED. For example, in patients with SRED presumably induced by obstructive sleep apnea, treatment of the obstructive sleep apnea with nCPAP may also control the abnormal nocturnal eating. In patients with SRED associated with RLS (or SW), treatment with a dopaminergic medication, at times combined with a benzodiazepine and/or benzodiazepine, can control both sleep problems.32,33 Interestingly, benzodiazepine monotherapy is rarely effective in controlling “somnambulistic eating.” Topiramate taken at bedtime is a promising new treatment of SRED.39 Cognitive-behavioral therapies and hypnosis are not usually effective in SRED.

TS 18.02
Polysomnographic findings in Sleep-Related Eating Disorder

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Aims: To assess the clinical and videopolysomnographic characteristics of the nocturnal eating episodes, the pattern of motor behaviours and their relationship to sleep structure in Sleep-Related Eating Disorder (SRED).

Methods: Thirteen consecutive drug-free patients with SRED underwent clinical interviews and VideoPolySomnography (VPS).

Results: Nocturnal eating episodes were associated with a history of sleepwalking, sleep-talking, restless legs syndrome (RLS) and periodic limb movements during sleep (PLMS). VPS showed 16 awakenings associated with eating behaviour in ten patients. Eating occurred during a complete awakening from NREM, never from REM sleep, characterized by alpha EEG activity. No dissociated features of sleep variables were observed. Patients interviewed during the episodes were conscious and able to remember the events the next day. PLMS were recorded in ten patients, RLS in five patients, associated in four with PLMS. Recurring chewing and swallowing during sleep were a feature in eleven patients, associated in over half of the events with EEG arousals.

Conclusions: In our patients sleep-related eating episodes were associated with other sleep disturbances (especially PLMS and RLS) suggesting a diagnosis of SRED. Eating episodes occurred with normal levels of wakefulness and recall. In addition to the PLMS, trigeminal-facial recurrent EMG activity due to chewing and swallowing movements is frequently encountered in SRED.

TS 18.03
Eating disorders during sleep: the Sleep Center Perspective

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Sleep-related eating disorder (SRED) is a heterogeneous syndrome, in which nocturnal arousals from sleep are
Movement (NREM) Parasomnias

Motor and Other Phenomena in Non Rapid Eye

TS 19.01
Motor and Other Phenomena in Non Rapid Eye Movement (NREM) Parasomnias

followed by rapid and compulsory eating behaviour. In the literature studies, individuals displayed reduced or more rarely full awareness during the episodes and usually had subsequent amnesia for the nocturnal eating episodes. Other reported characteristics are the following: female gender predominance, personal histories of other parasomnias, chronic course of the disorder. The relationship of SRED to other categories of sleep-related eating, in particular the nocturnal eating syndrome (NES), remains unclear. According to the International Classification of Sleep Disorders (ICSD), NES is defined as recurrent awakenings from sleep associated with an inability to resume sleep without eating or drinking. The presence of impaired consciousness and subsequent amnesia for the eating episodes was considered by some authors the major differentiating feature of SRED versus NES.

In the sleep centers of University Vita-Salute San Raffaele, Milano and University of Bologna, we have evaluated 35 consecutive patients (age range: 24–77 yrs; mean BMI: 28.5; mean age at onset of SRED: 39.6 yrs). All patients underwent a semi-structured clinical interview. In all patients SRED was the main clinical condition for which they sought referral. There was a preponderance of young females (21/35), and nocturnal eating episodes were reported every night, or almost every night, often many times per night. Additional reported categories of sleep disorders were sleepwalking in one patient, RLS in eight, PLMS in four and sleep talking in five. Mild mood depression was observed in fourteen patients. There was a positive family history of SRED in two patients, and psychiatric disorders (depression, eating disorders) plus SRED in two patients. Neurological examination and brain MR/CT imaging were always normal.

Our clinical-demographic data confirm previously reported features of SRED, including female gender predominance. However, all our patients had a clear recall of the nocturnal episodes in the morning. They were all drug-free, whereas most patients in the other case series were under psychotropic medications or had substance abuse. Therefore confusion and amnesia for the episodes, and even probably the careless and sloppy eating behaviour reported in the literature may relate at least in part to the confounding effects of medications or substance abuse. Based on our patients’ series, we may conclude that impaired levels of consciousness cannot be taken as the one feature clearly typifying SRED in comparison to the other nocturnal eating syndromes.


TS 19.02
Similarity and difference between REM sleep behavior disorder and REM sleep in normal infants

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Aims: To educate attendees of the symposium how to recognize and differentiate movements and behaviors due to incomplete sleep/wake arousals or sleep/wake transitions, from similar if not identical movements and behaviors of epileptic origin.

Methods: Similar movements and behaviors, occurring at sleep onset (wake/NREM sleep transitions), or in the middle of the sleep process (NREM sleep/wake transitions), captured by standard nocturnal video-polysomnography or electroencephalography will be contrasted by video presentations and discussed.

Results: Following movements/behaviors will be presented: 1. Wake/NREM Sleep Onset transition: Rhythmic Movement Disorder 2. NREM Sleep/Wake transition: Nocturnal Paroxysmal Dystonia 3. NREM-Delta Sleep/Wake transition: Sleep Terror

Conclusions: These movements and behaviors seem to be trapped in a “borderland” between sleep and wakefulness (prolonged and ineffective transition or “state dissociation”). Based on recent developments in understanding of sleep physiology, mutual inhibition of wake and sleep-promoting neurons seems to generate a bistable feedback loop that resists, small transient changes in the activity of either neurons, thus generally avoiding intermediate states. Destabilization of this feedback loop may underline abnormal sleep/wake transitions.

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REM sleep behavior disorder (RBD) is a parasomnia characterized by harmful or potentially harmful dream-enacting behaviors during REM sleep. There is a minimal diagnostic criteria for RBD provided in the International Classification of Sleep Disorders Revised (ICSD-R) which depends on only clinical manifestation, however, the interobserver reliability of the minimal diagnostic criteria for RBD is not satisfactory. As abnormality of muscle atonia during REM sleep has been considered to be a pathophysiological basis for RBD, in order to confirm the diagnosis, excessive augmentation of chin EMG or excessive chin or limb phasic EMG twitching should be demonstrated by PSG. Simultaneous video recordings of RBD patients usually reveal various features of behaviors/movements ranging from localized movements such as shaking or rotating the
head, grimacing, teeth clenching, bruxing, chewing, throwing out or raising an arm, waving a hand to full-blown clearly purposeful or highly elaborated behaviors from which one could imagine what the patients are doing in their dreams. In some cases, sleep talk ranging from mumbling, screaming, uttering a word to talking full sentences is documented associated with or without behaviors/movements. It is not difficult to make a diagnosis of RBD from the video so long as the behaviors/movements are typical and observed frequently as clusters with the cyclic appearance in accordance with expected REM cycle, but only minor, infrequent movements may require PSG confirmation. There has been accumulative evidence that RBD is often associated with or heralds the clinical onset of alpha-synucleinopathies. In this aspect, it is getting more and more important to be familiar with various clinical manifestation of RBD. The similar, but generally localized, phenomena are seen especially in the facial expression of normal infants or young children during REM sleep. They are of a smile, a grimace and amazement, but never with ambulation. We generally believe that muscle tone is profoundly suppressed during REM sleep, but there is a developmental change in the neuronal systems in the brainstem that suppress muscle activity during REM sleep. From the studies focusing on phasic components of REM sleep (i.e. rapid eye movements, muscle twitches) in infants and children of different ages, together with the observations about young mammals and primitive ones (i.e. the platypus), the human nervous system involved in muscle activity suppression during REM sleep is hypothesized to comprise at least 2 independent systems mediating tonic inhibition that is active throughout the REM sleep period, and phasic inhibition that acts in association with rapid eye movements. This hypothesis partly explains a wide variety of PSG features of REM sleep without atonia seen in RBD patients and the difference in behavioral manifestations, especially in patients with presumable extensive brainstem pathology.

**TS 19.03**

**Abnormal Motor Phenomenons in Sleep**

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There is a variety of abnormal motor phenomenons both in NonREM and in REM sleep, that occur in different diseases, such as neurodegenerative disorders, restless legs syndrome, parasomnias, and others. Parasomnias are defined as undesirable behavioral phenomena that occur predominately or exclusively during the sleep period. They can be classified according to the sleep state of origin: Parasomnias of non-REM (NREM) sleep (Arousal disorders, disorders of wake-sleep transition), parasomnias associated with rapid eye movement (REM) sleep, and other parasomnias (i.e., those not respecting sleep state).

In this seminar, video examples of a wide variety of abnormal movements during sleep including parasomnias, dyssomnias, and sleep disorders associated with neurodegenerative diseases will be demonstrated. Head banging (jactatio capitis) as rare, and bruxism as frequent phenomena will be discussed. Rhythmic teeth grinding (sleep bruxism) is the most frequent parasomnia, and may occur as a single disorder or be associated with other disorders of sleep and wakefulness, or rarely be associated with an epileptic motor event. Sleep bruxism (SB) is an unusual orofacial movement described as a parafunction in dentistry and as a parasomnia in sleep medicine. Examples of nocturnal chewing and smacking in patients with Parkinsonism are shown in NREM sleep. Somnambulism and pavor nocturnus represent further behavioural abnormalities of parasomnias.

Simple motor events are periodic limb movements in sleep, often associated with the restless legs syndrome or neurodegenerative diseases or narcolepsy. They are defined by frequency, periodicity and intermovement interval according to the ASDA and occur in sleep stage 1 and 2, also during the wake stage, rarely in stage REM or deep sleep. More complex movements are excessive hypnic jerks at the onset of sleep, in severe cases demonstrated as propriospinal myoclonus at sleep onset, that can comprise several body regions or the whole body.

**TS 19.04**

“Paroxysmal nocturnal dystonia”, epileptic seizures

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The clinical relevance of Nocturnal Frontal Lobe Epilepsy (NFLE) has been underlined in the last years. This syndrome represents a spectrum of clinical manifestations, ranging from brief, stereotypic, sudden arousals, recurring often several times per night, sometimes with a quasi-periodic pattern, to more complex dystonic-dysskinetic or hyperkinetic seizures and to prolonged somnambulic behaviour. Episodes of different intensity have been labelled as Paroxysmal Arousal (PA), Nocturnal Paroxysmal Dystonia (NPD) and Episodic Nocturnal Wandering (ENW). Interictal and ictal scalp EEG are often normal and the clinical history is often aspecific to really differentiate possible seizures during sleep from non-epileptic attacks (as parasomnias and in particular arousal disorders). Since for most of the patients deep electrode (invasive) recordings are not possible, video-polysonographic recording are of utmost importance for diagnosis and for categorization of the motor and behavioural episodes during sleep. NFLE with its different manifestations (PA, NPD and ENW) should be suspected in the
presence of frequent, repetitive, abrupt-onset and stereotypic paroxysmal nocturnal motor events arising from sleep and persisting into adulthood. Video-polysomnography is mandatory to confirm the diagnosis.

**TS 20: Sleep Disorders and Attention Deficit-Hyperactivity Disorder**

**TS 20.01**

**Attention Deficit-Hyperactivity Disorder and co-morbid disorders: a rationale for treatment**

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Early researchers found little sleep disruption in Attention Deficit-Hyperactivity Disorder (ADHD) until they began to study the associations of ADHD with other sleep disorders such as Obstructive Sleep Apnea (OSA), Nocturnal Seizures, Narcolepsy and Restless Legs/Periodic Limb Movements in Sleep (RLS/PLMS).

From a theoretical point of view, these disorders can either exacerbate the symptoms of idiopathic ADHD or cause de novo symptoms of inattention and hyperactivity thus mimicking the symptoms of idiopathic ADHD. From the clinical point of view, an attempt should be made to discriminate between these possibilities although, in either case, treatment of the underlying sleep disorder may lead to improvement in the ADHD symptoms. The evidence is strongest for this in OSA.

Other speakers have covered the fundamentals of the connection of these disorders to ADHD except for Narcolepsy. In a recent review of 14 studies that examined cognitive dysfunction in patients with Narcolepsy, neuropsychological impairments included impaired sustained attention, vigilance and driving simulation performance. In a study of 19 patients with Narcolepsy and 20 controls, one group of authors concluded that some of the deficits in attention in patients with Narcolepsy may be temporally related to drowsiness, but the same authors elicited evidence from the study that there may be independent reasons for the deficits in attentional capacity and attentional control in Narcolepsy that are intrinsic to the Narcolepsy itself.

In future studies, more rigorous neuropsychometric studies need to be done to show what aspects of the attentional matrix improve with stimulant therapy in Narcolepsy. An NIH funded double-blind study is being conducted to verify that dopaminergic therapy is effective in treating ADHD symptoms in children with and without RLS/PLMS. A causal link between PLMS and the symptoms of ADHD remains to be established.


**TS 20.02**

**Obstructive sleep apnea syndrome (OSAS) in Attention Deficit Hyperactivity Disorder (ADHD): when and how does it contribute**

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There are complex relationships between ADHD and sleep disorders starting from clinical standpoints: children diagnosed with ADHD have high rates of subjective sleep complaints and some evidence of sleep disturbances; children obtaining insufficient sleep or with sleep disruption frequently show signs of inattentiveness and sometimes of hyperactivity; stimulants used to treat ADHD may interfere with sleep; behavioural problems associated with ADHD can interfere with bedtime organization and scheduling. Otherwise, i.e. inattention and hyperactivity are frequently reported in children with sleep-disordered breathing (SDB), with resolution after treatment. Different studies gave power to the hypothesis that SDB does contribute to ADHD also if a direct relationship has not definitely demonstrated. The increased prevalence of habitual snoring, suspected apnea and sleepiness in children with hyperactivity index of the Conners’ Parent Rating Scale or an high score in an inattention/hyperactivity scale from one hand, and an high ESS and higher Conners score in children with recorded SDB compared to controls from the other hand seem to suggest a possible causative link between the two disorders. However longitudinal epidemiological data are lacking. Cross-sectional studies showed by polysomnography that 6–12 aged children with ADHD have an increased prevalence of apnea-hypopnea index >1 respect with matched controls, but the criteria for ADHD based on the DSM-IV do not differentiate between children with or without sleep disorders. A recent paper examining a large cohort of 5–7 aged children by a questionnaire and night polysomnography found that OSAS was present in 5% of those with significant ADHD symptoms, 26% of those with mild symptoms and 5% of those with no symptoms. Moreover REM disturbances were more
frequent in overt ADHD with possible effect on daytime neurobehavioural functioning. The possible conclusion is that the prevalence of OSAS in ADHD is not different from that of the general pediatric population, but SDB may contribute to some mild ADHD-like symptoms that can be readily misperceived and the theoretical basis of overlap between the two diagnoses.

**TS 20.03**  
**RLS and PLM in pre-pubertal children**  
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Restless Leg (RLS) and Periodic Limb Movements are often not considered in pre-pubertal Children. We performed a study on all successively seen and monitored prepubertal children referred for a sleep disorder to a sleep clinic. We had systematic search for presence of RLS, and possible symptoms associated with PLM for a 12 months period. 292 children (96 girls), mean age 7 years 1 month, range 15 months-11 years, interfered the study. All children were Tanner stage1 and none was refereed for RLS or suspicion of PLM. The causes for referrals were excessive daytime sleepiness or disturbed nocturnal sleep with or without behavioral problems or parasomnia. Two children presented with RLS and associated PLM at polysomnography, none had a positive family history of RLS. Including these 2 cases, 58 children (23%-23 girls; presented ‘periodic leg movements’, but only 2children (0.8%) had isolated PLM and complaint of sleep disturbance. The most common association was sleep disordered breathing (SDB) (n = 29), even when efforts was made not to count PLM related to abnormal breathing. SDB was also associated with neuro-muscular disorders, GE reflux and asthma and other co-morbid problems. Twenty children had association with neuro-psychiatric syndromes (RLS, narcolepsy, nocturnal seizure, ADHD, cerebral palsy, myotonic dystrophy). Children with these disorders may have had several co-morbidity (example cerebral palsy and GE-reflux). All other syndromes were treated first. Children with and without PLM at PSG were compared; and treatment trials tried to first address the other sleep disorders and co-morbidity. No difference in age and gender distribution was seen between children with and without PLM, and there was no prominence of a specific co-morbidity in the PLM group compared to the non PLM group. Treatment of SDB, most frequent co-morbid association, controlled PLM in 15/29 children independent of associated other co-morbidity, but SDB was well controlled in only 23/29 children with surgery. At the end of treatment adjustments, 6 children were considered for pharmacologic treatment with a dopamine agonist, pramipexol. These children included 2 children with RLS and PLM, 2 children with isolated PLM and 2 children with well treated SDB, absence of other co-morbidity and persistence of PLM and clinical complaint. Five/6 tolerated well the treatment and had control of PLM at PSG and disappearance of subjective complaints. One subject discontinued the drug due to side-effect. Even if PLM are fairly commonly seen in PSG of prepubertal children, there pathological significance can be unclear. In some cases they may be consequence of the abnormal chronic sleep and in other but more rarely they may be the cause of the sleep disturbance.

**TS 20.04**  
**Nocturnal seizures and disorders of arousal in ADHD**  
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ADHD co-morbidity with epilepsy has been known and frequently reported in the adult population. The association with focal seizures from the frontal or temporal lobe seems to be more frequent in the adult population. As for ADHD children, an increased frequency of rolandic spikes has been recently reported (1). Seizures reports prevail in the inattentive ADHD subtype, either generalized or complex partial seizures from the frontal lobe. Interictal epileptic discharges (IEDs) are by far more common than seizures in ADHD children and their reduction under antiepileptic treatment improves alertness and sustained attention (2). There are quite few reports about sleep disruption in ADHD, especially sleep related breathing disorders (SRBD), restless leg syndrome (RLS) and periodic leg movements during sleep (PLMS).

No reports exist about nocturnal seizures in children with ADHD and very few about non epileptic paroxysmal events at night such as disorders of arousal (DOA) (3), partially due to the paucity of video-polysomnographic recordings obtained.

We recently evaluated 12 male children, mean age 8.25, range 4–13, with full video-polysomnography including 18 EEG leads (10–20 system) and found 9/12 recordings positive for IEDs; only 4 patients had positive wake EEGs. IEDs were bilateral in 7, predominantly rolandic (5 children) or bifrontal, unilateral in 2 with an overall predominance of left IEDs. Nocturnal hypermotor seizures were recorded in 2 children with a total of 10 episodes, of which 6 were paroxysmal arousals. Besides a very high percentage of PLMS (8/12) and RLS (4/12), parasomnias were highly represented in this group, especially DOA (5/12) and among them confusional arousals were the most common. Many times from videos alone, they could be misdiagnosed as nocturnal seizures and they seem to be associated with a high percentage of SWS (mean 33% of TST).

Levetiracetam at therapeutic dosing improved clinical sleep, with disappearance of both seizures and DOA and
reduction of IEDs, paralleled by improvement of beha-

culional and cognitive testing.

References


TS 21: Neurobiology of Insomnia-Relevance for diagnosis and treatment?

TS 21.01
Retrospective Study of Sleep Characteristics of 100 Patients with Primary Insomnia: Concluding Results

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Aims: A lot of research has been done concerning the polysomnographic (PSG) sleep of patients with insomnia complaints in general. When it comes to “primary” insomnia though, there are only few studies using PSG measures, when focusing on this specific type of disturbed sleep. The reason for this lack of studies might be previous findings, in which primary insomnia patients reported of greater sleep disturbances than could be found via PSG. In our retrospective study of a large sample of primary insomnia patients we therefore explored not only objective differences between patients and healthy controls. We additionally examined subjective sleep characteristics in comparison to objective measures, influences of gender and age on sleep, as well as differences between the nights, hypothesizing different changes from the adaptation to the baseline night between insomniacs and controls.

Methods: A sample of 100 insomniac patients (INS; 46 men and 54 women, age-range: 17–65 years, mean: 42.57 ± 12.50 years), all of them being free of hypnotic drugs for at least two weeks before sleep laboratory examination, was compared with 100 healthy subjects (CON; 46 men and 54 women, age-range: 20–79 years, mean: 41.12 ± 13.99 years). For subjective estimates of sleep parameters we used a sleep questionnaire which was filled in by the subjects in the morning shortly after waking up. For statistical analysis of group effects we performed MANOVAs with the factor GROUP and GENDER and the covariate AGE, separately on the set of polysomnographic and subjective parameters. Multivariate statistics were based on Wilk’s Lambda. p<.05 was considered to be significant.

Results: INS differed significantly from CON in terms of a reduced total sleep time (TST) and sleep efficiency (SE), a higher arousal index and more awakenings. Additionally, INS exhibited significantly less wake% and REM% than CON. By looking at the factor GENDER, only stage 1 and slow wave sleep (SWS) differed between INS males and INS females significantly. None of these differences appeared in the healthy control group. TST, SE, SWS% and REM% all significantly decreased with age. REM latency and number of eye movements were also reduced with age. On the other hand, the number of awakenings, the arousal index as well as wake% and stage 1% increased with age. When evaluating subjects’ estimates of sleep by comparing objective and subjective sleep onset latency (SOL) as well as subjective and objective TST we found moderate correlations for SOL (r = .520, p = .000) and TST (r = .391, p = .000) for CON. INS showed smaller correlations for SOL (r = .344, p = .001) and TST (r = .348, p = .001).

Discussion: The above mentioned and further results will be discussed during the presentation.

TS 21.02
Spectral analysis of the sleep EEG in primary insomnia-A neurocognitive theory of insomnia

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Insomnia is roundly considered a disorder of hyperarousal. That is, the patient with insomnia has a level of arousal that is incompatible with the initiation and/or maintenance of sleep. The concept seems as simple as it is obviously true. If, however, subjected to a reasonable level of scrutiny, it becomes evident that the concept of hyperarousal is likely to be quite complex.

What is meant by arousal? How does it become elevated? Is hyperarousal a tonic phenomena and if not, what factors mediate and/or moderate its occurrence and/or intensity? Finally, is it even likely that arousal is a singular construct and, if it is, is it necessarily the case that hyperarousal and sleep are mutually exclusive phenomena?

In the present lecture we review one model (and the evidence for it) which addresses these issues. In brief, the model is referred to as the Neurocognitive perspective. It suggests that (1) hyperarousal needs to be considered as a heterogeneous phenomena (comprised of somatic, cortical, and cognitive arousal); (2) that cortical arousal (as opposed to somatic arousal and/or cognitive arousal) is primarily responsible for sleep initiation and maintenance problems in patients with Chronic Insomnia; and, (3) cortical arousal itself is only a correlate of the phenomena of interest. That is, it has been hypothesized that cortical arousal is
permissive of levels of sensory and information processing which:

- when the individual is awake, makes it difficult to disengage from the environment and initiate sleep,
- when the individual is asleep, makes it more likely that the individual will awaken, and
- when the individual remains asleep, makes it more likely that the individual will not perceive sleep “as sleep”
- The data which support the perspective shows that patients with insomnia
- have reduced arousal thresholds
- exhibit increased levels of cortical arousal, as measured by High Frequency EEG activity (HFA)
- exhibit a correlation between HFA and the occurrence of subjective-objective discrepancy (sleep state misperception) and self-reported poor sleep quality
- tend to exhibit an attenuated sleep-related mesograde amnesia.

TS 21.03
Neuroendocrine and neuroimmunological investigations in primary insomnia

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Primary/psychophysiological insomnia is conceptualized as a 24-hour hyperarousal disorder. Attempts have been made to characterize the hyperarousal in terms of central nervous measurements including spectral analysis of the sleep EEG, but also parameters of the neuroendocrine and neuroimmune system. Own research investigated the nocturnal excretion of cortisol, growth hormone, melatonin, neuropeptide substance P, leptin and interleukin-6 from 19:00 to 9:00 hours continuously in comparison to age- and gender-matched healthy controls. Contrary to expectation in two independent studies (sample sizes: 1st study: n = 10; 2nd study: n = 11) in patients with primary insomnia no increase of cortisol was observed in our patients. The same held true for growth hormone secretion. In the first study decreased melatonin secretion was found in our patients with insomnia and in the second study an increased secretion of interleukin-6 especially during the second half of the night was noted. These heterogenous results are difficult to interpret in the context of other studies which demonstrated an activation of the HPA-axis in insomnia. Unexpectedly, cortisol as a marker of the stress system and of the HPA-axis was not enhanced as predicted which might be related to specific characteristics of our samples. On the other hand, increased IL-6 excretion in our insomniac sample may point to an impact of chronic disturbed sleep on the immune system. With respect to leptin no difference between control subjects and patients were documented thus not supporting the hypothesis that disturbed sleep leads to obesity by decreasing leptin secretion.

TS 21.04
On the process of falling asleep-studies with combined fMRI and EEG

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Since many decades, the EEG plays a pivotal role in the assessment of vigilance states of the brain. However, the functional correlates of the oscillatory processes that determine much of the ongoing EEG-those EEG properties most often used to assess vigilance-are only superficially understood. The simultaneous acquisition of EEG and functional MRI has recently opened new possibilities to examine the cortical and subcortical correlates of EEG-derived vigilance parameters.

In a pilot study in seven healthy subjects, we have recently found correlates of EEG alpha fluctuations in mesencephalic and thalamic areas. The thalamic correlations included the centromedian and intralaminar nuclei; The mesencephalic-medial thalamic network, rather than generating individual waves, apparently has a leading role in the modulation of alpha activity and probably also vigilance. In the current study, we address theta in addition to alpha waves during increased sleepiness as well as applications to yield information upon the neurobiology of sleep onset insomnia.

TS 22: Periodic leg movement in sleep: old questions-new insights

TS 22.01
New criteria proposal for Periodic Leg Movement scoring

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Introduction: The criteria for scoring Periodic Leg Movements (PLMs) during sleep were established on the basis of the visual analysis of the tibialis anterior muscle
EMG recording. Even if these criteria were based on the observation of a large number of polysomnographic recordings, a clear and reliable statistical approach was not described. Moreover, the use of computer-based recordings makes it now possible to use more refined analyses of the different parameters which can be calculated from digitally-recorded LMs. For this reason, the aim of this study was to quantify and analyse the sleep motor patterns of normal controls and of patients with RLS/PLM by using criteria which allowed also the inclusion of motor events usually not considered by the classical criteria for scoring PLMs.

Method: For these reasons all EMG bursts were detected with a duration between 0.5 and 15 s; the threshold used was 10 µV (with resting EMG tracings consistently below 2 µV) from both anterior tibialis muscles. Events were considered as separate when an interval of at least 0.5 s was found between them. The same interval was used for the definition of monolateral or bilateral LMs. For each LM, the interval from the preceding LM (onset-to-onset), duration and area under the curve (µV/s) were measured.

Results: We analysed the distribution of inter-LM intervals by plotting their distribution histogram with classes for <2 s to 100 s, and steps of 2 s. Young normal controls showed a main peak at 2–4 s rapidly decreasing to values close to 0 at 10 s; the patients with RLS and PLM showed 2 main peaks, one at <2 s and another at around 20–24 s, with a dip at around 8–10 s. On the basis of the idea that 2 distinct LM categories were present in this graph, one periodic (20–24 s) and another as an exaggeration of the normal peak at 2–4 s, we established a so-called “periodicity index” or PI = number of sequences of 3 intervals ≥ 10 ≤ 90 s/total number of intervals. On the basis of this index we identified 3 subgroups of patients each with a range of PI, corresponding to different distribution of inter-LM intervals: PLM1, with PI ≥ 0.75 and only the peak at 20–24 s in the inter-LM interval histogram; PLM2, with PI ranging between 0.55 and 0.75 and both peaks (2–4 s and 20–24 s) in the histogram, and, PLM3, with PI < 0.55 and only a main peak at 2–4 s. The contemporary use of the total LM index and PI allowed us to differentiate clearly these 3 subgroups between them and from the normal controls; this was not possible by using only the classical PLM index.

Conclusion: These results seem to indicate that the classical PLM index might be insufficient to characterize the complex LM patterns of patients with RLS and PLM and a more detailed approach like ours might disclose the presence of 2 different categories of LMs, in different proportions; probably, only one of these categories is under dopaminergic influences.

TS 22.02
Actigraphy in PLM monitoring
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Aims: Several actometers with specific software to detect periodic limb movements (PLM) are available and increasingly used to assess treatment effects on PLM in patients with Restless Legs Syndrome (RLS). We evaluate the correlation between PLM counts obtained with polysomnography (PSG) using standard scoring criteria and PLM counts derived from 2 different actometers.

Methods: 24 patients (mean age 57.5 ± 12.0 years) with a PLM index (PLMI) > 5 per hour in a previous PSG participated in the study; 12 had RLS/PLMS, 12 had PLMS without RLS. All patients underwent a full night (8 hours) of digital PSG and simultaneous actigraphy from both legs (Actiwatch with PLMS Software V.2.36, Cambridge Neurotechnology UK). In addition to 10 of those patients were examined simultaneously with a second actometer (PAM-RL with Software Version 7.5.3, ImSystems). For analysis, PSG and actigraphy were displayed in simultaneous 1 minute windows. In PSG, PLM were manually counted according to standard criteria (Sleep 1993;16:748–759). Actigraphic PLMI were obtained automatically for TIB.

Results: For the 24 patient the polysomnographic PLMI was 34.4 ± 30.7 PLM/hour (h) time in bed, the PLMI with Actiwatch actigraphy was 21.2 ± 25.6 PLM/h TIB (p < 0.001, Wilcoxon test). Only 61.6% of the PLM in PSG were detected by the Actiwatch. However, there was a high correlation of PSG and Actiwatch actigraphy derived PLMI (Spearman’s correlation coefficient r = 0.835, p < 0.001). For the 10 patient the polysomnographic PLMI was 37.0 ± 30.7 PLM/h TIB; the PLMI with PAM-RL actigraphy was 63.6 ± 39.3 PLM/h TIB (p = 0.009, Wilcoxon test). A high correlation of PSG and PAM-RL actigraphy derived PLMI was found (Spearman’s r = 0.939, p < 0.001).

Conclusions: The Actiwatch actigraphy significantly underestimated PLM counts, whereas the PAM-RL actigraphy significantly overestimated PLM counts in comparison with PSG. However in both types of actigraphy we found a high correlation between polysomnographic and actigraphic PLMI. This may relate to the fact that EMG activation of the tibial anterior muscle is used to identify PLM in PSG, and manifest movement of the limb in actigraphy. The high correlation between PSG and actigraphic PLMI indicates nevertheless, that actigraphy is useful to identify PLM. PSG and different types of actigraphy cannot be interchanged when doing follow-up studies.

TS 22.03
Impact of PLMS on sleep quality
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Objective: Periodic leg movements in sleep (PLMS) are a common finding in various sleep disorders. Whether PLMS
are causally related to the presence of sleep-wake disturbances is still being debated. Previous studies investigating the subjects’ degree of daytime sleepiness and their self-estimated severity of insomnia could not find a relationship between these parameters and PLMS indices. Not cleared yet either to which extent PLMS alter the cortical EEG activity compared to PLMS which are associated with arousal and contribute this way to non-restoring sleep. To explore these questions, we investigated the relationship of the occurrence of PLMS to patients’ perception of sleep quality during a night of polysomnography in various sleep disorders and performed spectral analysis of the sleep EEG in patients with restless legs syndrome (RLS).

Results: Subjective sleep quality did not correlate with the PLMS indices. In the spectral analysis, PLMS alone had only a minor and transient effect on the EEG spectra. Contrarily, PLMS associated with arousal and arousals resulted in significant increase of higher EEG spectra (alpha, beta1, beta2 and gamma bands).

Conclusions: PLMS appear to have a low impact on the subjects’ perception of sleep quality and on the sleep EEG spectra. The presentation will give an overview on studies exploring the role of PLMS in sleep disorders.

**TS 22.04**

Periodic Leg Movements in Sleep (PLMS) in Narcolepsy, REM Sleep Behavior Disorder and Normal Controls

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While PLMS were first documented in patients with the restless legs syndrome (RLS), they were also reported in patients with various sleep disorders as well as in normal subjects especially with advancing age. This presentation will focus on prevalence, electromyographic (EMG) characteristics and functional significance of PLMS in three different populations, namely narcolepsy, REM sleep behavior disorder (RBD) and normal individuals. Results obtained recently in our laboratory show that PLMS are more frequent in narcolepsy or RBD than in normal controls and more than 70% of narcoleptic or RBD patients have a PLMS index higher than 5. When present in normal subjects, PLMS have the same EMG characteristics than in RLS, narcolepsy or RBD. However PLMS seen in normal subjects have little impact on nocturnal sleep organization but are associated with autonomic activation as previously reported in patients with RLS. Patients with RBD or narcolepsy have a low percentage of movements associated with micro-arousals and a decrease amplitude of the EKG response associated with PLMS. These results suggest the possibility of autonomic dysregulation in RBD and in narcolepsy.

**TS 23: Clinical and technical advances in CAP application**

**TS 23.01**
The role of CAP in the physiology and ontogeny of sleep

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The default state of the sleeping brain is a complex system of numerous self-governed oscillations. Besides the slow <1 Hz rhythm of non-REM (NREM) sleep, a large body of literature has demonstrated infraslow fluctuations (0.02–0.05 Hz) during sleep affecting the EEG power, phasic events, epileptic abnormalities and sleep disorders with periodic manifestations. These observations have raised the evidence that during sleep the brain generates cyclic changes in cortical and/or subcortical excitability, which are able to recruit very large neuronal networks. CAP (cyclic alternating pattern) is the detectable expression of infraslow oscillations based on a 20–40 second swing between an activating phase A and a deactivating phase B. Like a “brain beat”, CAP synchronizes neuronal groups and drives the state progression across non-REM sleep. Every CAP cycle (phase A + phase B) can be considered as a functional segment that step by step builds-up the evolution of the sleep profile. The modulation of these effects is carried out by a hierarchy of different CAP phase A subtypes, which ranges from sleep promoting cerebral activation (subtypes A1), to a balanced mixture of both sleep-promoting and sleep-disrupting features (subtypes A2), to overt arousal (subtypes A3 and EEG arousals). The amount and time distribution of the different phase A subtypes and arousals have implications on the sleep homeostatic and ultradian regulatory mechanisms. The declining slope of the amount of phase A1 across the consecutive sleep cycles parallels the exponential reduction of slow wave sleep (SWS). The positive correlation between subtypes A1 and SWS suggests that subtypes A1 (K-complexes and delta bursts) are the forerunners of deep NREM sleep and correspond to the oscillations inducing progressive amplitude increase of the EEG signal linked to the build-up and maintenance of SWS. In contrast, phasic fast activities (FA), i.e., subtypes A2, A3 and arousals, remain almost unmodified in the consecutive sleep cycles. The peaks for FA prevail during the pre-REM periods of light NREM sleep and during REM sleep. Across the life span, subtypes A1 decrease from adolescence to adulthood followed by a random distribution in the second half of life. In contrast, FA show an age-related positive linear profile.
The coexistence in CAP of both slow (subtypes A1) and rapid (FA) EEG patterns across the life span accounts for the age-dependent profile of CAP rate (ratio of CAP time to NREM sleep time), resulting from the prevalence of EEG synchronization in the first half of life and from the rise of FA in the second half when slow wave activity declines. In conclusion, CAP subtypes and arousals are woven into the basic mechanisms of sleep regulation and undergo specific age-related modifications. Within the sleep architecture, subtypes A1 show an exponential decline across the successive sleep cycles, according to the homeostatic process. In contrast, the distribution of FA is not influenced by the order of sleep cycle, but by the ultradian rhythm with periodic peaks of FA occurring before the onset of REM. The dynamics of CAP and arousals during sleep reflect the decay of the homeostatic process and the interaction between REM-off and REM-on mechanisms.

The power spectrum analysis of CAP subtypes A1 shows a dominant peak in the frequency range of 0.25–2.5 Hz. The topographic scalp mapping performed in these frequencies during phase A1 shows a clear prevalence over the anterior frontal regions. The regions involved coincide with the origin of spontaneous and evoked K-complexes. In effect, a great portion of the power spectrum in subtypes A1 falls into the range of <1 Hz slow oscillation. For this reason it has been suggested that the bursts of subtypes A1 have a grouping effect on cerebral <1 Hz slow oscillation. Compared to subtypes A1, subtypes A2, A3 and arousals show different frequency band aggregation and topographic cortical mapping. In subtypes A2 there is a combination of 2 peaks: the first in the range of 0.25–2.5 Hz and the second, smaller, including theta and alpha activities. In subtypes A3 and arousals there is a dominant peak around 9 Hz. The topography the FA shows a clear prevalence over the parieto-occipital areas.

### TS 23.02
Neural mechanisms of CAP in EEG synchronization processes

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The cyclic alternating pattern (CAP) translates a condition of sustained arousal instability oscillating between a high (phase A) and a low level (phase B). We have shown that there is a deterministically generated time structure of these arousal fluctuations during sleep which might be driven by external sensory inputs but autonomously predispose the brain to be less or more influenced by the environment and CAP is the EEG phenomenon describing this process. CAP is based on the complex spatial-temporal interaction between two different main frequency components. The first, in the delta frequency range, seems to be generated in the frontal brain structures while the second, with frequencies ranging between 7 and 15 Hz, is located more posteriorly, in the parietal and occipital areas. In order to study the dynamics of spatial synchronization of the slow-wave activity recorded from different scalp electrodes during sleep we characterized the different levels of EEG synchronization (in the 0.25–2.5 Hz band) of 5 healthy subjects by means of the synchronization likelihood (SL) algorithm and analyzed its long-range temporal correlations by means of the detrended fluctuation analysis (DFA). We found higher levels of interregional synchronization during CAP sleep than during nonCAP with a small but significant difference between its A and B phases. SL during CAP showed fluctuations probably corresponding to the single EEG slow-wave elements. DFA showed the presence of 2 linear scaling regions in the double-logarithmic plot of the fluctuations of SL level as a function of time scale. This indicates the presence of a characteristic time scale in the underlying dynamics which was very stable among the different subjects (1.23–1.33 s). We also computed the DFA exponent of the 2 scaling regions; the first, with values ≈1.5, corresponded to fluctuations with period 0.09–0.75 s and the second, with values ≈1, corresponded to fluctuations with period 1.5–24.0 s. Only the first exponent showed different values during the different sleep stages. All these results indicate a different role for each sleep stage and CAP condition in the EEG synchronization processes of sleep which show a complex time structure correlated with its neurophysiological mechanisms. Very slow oscillations in spatial EEG synchronization might play a critical role in the time long-range EEG correlations during sleep which might be the chain of events responsible for the maintenance and correct complex development of sleep structure during the night.

### TS 23.03
Use of CAP in understanding and treating sleep-disordered breathing

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### TS 23.04
Computerized CAP scoring: field validation

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Insomnia

O 001
Cognitive behavioral treatment for chronic insomnia with general anxiety disorder

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Cognitive behavioural therapy (CBT) is based on the cognitive model, which hypothesizes that people’s emotions and behaviours are influenced by their perception of events as follows: situation → automatic though → emotion. In a specific situation, one’s underlying beliefs influences one’s attitudes and emotions. Using this model, we hypothesized that automatic thoughts in chronic insomniacs with general anxiety disorder (GAD) can influence sleep and lead to a physiological response, difficulty in falling and/or maintaining sleep. This study consisted of 20 patients suffering from chronic insomnia and anxiety of at least one year’s duration. Patients initially underwent 2 consecutive polysomnography nights, filled out the Hospital Anxiety and Depression scale, Pittsburgh sleep Quality index, Beliefs and Attitudes about Sleep scale. They also showed abnormal features in Cloninger personality tests (high harm avoidance). CBT was based on treatment described by Beck and Emery and a relaxation tape with instructions on its use. This complete protocol involved two evaluations sessions and ten therapy sessions spread over a 12-week period. Treatment component includes: sleep information, stimulus control, sleep restriction, cognitive restructuring (thought restructuring), managing anxiety and intrusive thoughts. Anxiety management training consisted of detailed instruction on relaxation methods and how to use and controlling these in anxiety-provoking thoughts and images and increasing self confidence. We found that cognitive-behavioural therapy was effective in the treatment of chronic insomnia having GAD: total sleep increased, sleep latency decreased. During CBT the number of waking during the night decreased. Finally all patients initially using benzodiazepines remained drug-free.

Cognitive behavioural therapy is definitely effective in the treatment of insomnia associated with mental comorbidity such as GAD.

O 002
Stress-related Sleep Disturbance and Response to Caffeine

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Aims: To determine the polysomnographic (PSG) based response to caffeine in individuals vulnerable to stress-related sleep disturbance.

Methods: Subjects were 21 healthy individuals who did not have insomnia. Data were collected on 11 individuals selected based on low and 10 individuals selected based on high scores on the Ford Insomnia in Response to Stress Test, (“FIRST”; a measure of vulnerability to stress-related sleep disturbance). A low-dose of caffeine (3 mg/kg) was administered 1-hour prior to lights out and compared to a counterbalanced no-caffeine night with each condition separated by 1 week. Standard PSG measures were assessed (i.e., latency to persistent sleep, sleep efficiency, etc.).

Results: Age and gender were comparable between groups (p > .05). While there were no group differences in any PSG variable on the non-caffeine night. Individuals in the high FIRST group had a significantly longer latency to persistent sleep in response to the caffeine challenge (p < .05) (Figure 1).

Conclusions: Non-insomniac individuals with a self-reported predisposition to sleep disturbance, based on FIRST scores, had greater PSG sleep disturbance in response to a pharmacological challenge whereas baseline sleep was not different between groups. These results suggest that the construct of individual differences in vulnerability to sleep disturbance applies to a pharmacological “stressor” (i.e., caffeine) as well as previously assessed stressors such as a first night effect. Further research is needed to determine the relevance of this vulnerability to the future development of chronic insomnia in this population.

Support: National Institute of Mental Health Grant 068372 awarded to CLD No significant financial interest/other relationship to disclose.

Fig. 1.
**O 003**

**Sleep Disturbances, Oxidative Stress and Cardiovascular Risk Parameters in Postmenopausal Women complaining of Insomnia**

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**Aims:** Sleep complaints increase after menopause. It has been reported that 63% of postmenopausal women had insomnia. Sometimes they complain of insomnia and have another sleep disturbance such as apnea or periodic leg syndrome. Postmenopausal women are also at risk for health problems related to estrogen deficiency, such as cardiovascular disease. Homocysteine (Hcy) concentration has been shown to be an independent factor for cardiovascular disease. It is also reported to be related to estrogen status. Recent studies have documented that estrogens are potent antioxidants. The aim of this work was to investigate cardiovascular risk factors and oxidative stress parameters as well as sleep disturbances accessed by polysomnography in 38 Brazilian postmenopausal women (age varying from 50 to 65 years old) with insomnia.

**Methods:** For sleep analysis polysomnographs had been conducted. The oxidative stress parameters were analyzed by measuring blood concentration of catalase, superoxide dismutase (SOD), thiobarbituric acid (TBARS) and total glutathione (GSH) using spectrophotometric methods. As cardiovascular risk factors we measured plasma levels of Hcy, folic acid and B6-vitamin by HPLC methods. The study received the approval of Ethics Committee of UNIFESP.

**Results:** The polysomnography revealed: 68% (26 patients) had sleep efficiency decreased (lower than 85%), 50% (19 patients) had apnea. 7.8% (3 patients had periodic leg movements), and one patient had bruxism. The mean (± SD) concentrations for the parameters studied were: Catalase-82.45 ± 22.9 U/mgHb; SOD-13.87 ± 1.9 U/mgHb; GSH-6.16 ± 1.1 μmol/gHb; TBARS- 2.57 ± 0.9 nmol/mL; Hcy-11.7 ± 2.6 μM; B-6 vitamin-21.82 ± 4.5 nmol/mL; Folic acid-8.91 ± 1.6 nmol/mL.

**Conclusion:** Although all women had the complaint of insomnia, 50% of them had criteria of apnea at the polysomnography. Our results showed that the majority of the subjects presented normal concentrations of the parameters studied according to the standards reached on our laboratory, except from TBARS. In this case, only 9 women are under normal values.

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**O 004**

**FIRST Scores in Insomniacs and Controls**

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**Aims:** The Ford Insomnia Response to Stress Test (FIRST) is a validated questionnaire used to assess vulnerability to sleep disturbance in response to stress. Previous studies were done in individuals without insomnia. Thus, the question remains whether or not the FIRST differs in individuals with current insomnia and controls.

**Methods:** Seven hundred and sixty-three individuals were assessed with a 20-minute phone interview (mean age = 45.2 ± 12.1 years; 55.7%F). Initially, participants were divided into 4 disease groups: healthy subjects (n = 278), medical disease (n = 314), psychiatric disease (n = 41), and both medical and psychiatric disease (n = 130). Each of the disease groups, were then divided into individuals with insomnia and without insomnia making a total of 8 groups.

**Results:** A two factor ANOVA was used to analyze mean FIRST scores in the 8 groups. Across all disease states, insomniacs scored significantly higher than normal participants (main effect of insomnia, p < .001; Figure 1). A main effect of disease was also present (p < .05). Specifically, individuals with medical disease (p < .01) and those with both medical and psychiatric disease (p < .001) scored significantly higher on the FIRST than healthy subjects (Figure 2). There was no disease by insomnia interaction. Results were similar after co-varying for age and gender.

**Conclusion:** Insomniacs scored higher on this measure of vulnerability to sleep disturbance than normals. Interestingly, insomniacs have a higher FIRST score regardless of the nature of their insomnia (i.e. even after controlling for co-morbid conditions). Increased scores in the psychiatric and medical disease samples support the notion of elevated risk for insomnia associated with these conditions.

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**O 005**

**Effect of Warm Foot Bathing on Body Temperature and Sleep in Taiwan’s Elders with Sleep Disturbance**

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**Aims:** To test the feasibility of a warm footbath before sleep onset to alter core (rectal) body temperature, the distal (foot)-proximal (abdominal) skin temperature gradient (DPG), polysomnographic (PSG) sleep and perceived sleep quality in Taiwan’s community dwelling older adults complaining of sleep disturbance.

**Methods:** A randomized crossover design was used in this study. Fifteen older adults (9 women, 6 men, mean age = 64.7 years) with Pittsburgh Sleep Quality Inventory scores of > 5 had standard polysomnography (PSG) recorded for 3 nights. A 41°C warm footbath for...
40 minutes was administered before usual bedtime randomly on night 2 or night 3. Rectal and abdominal temperatures were recorded at 1-min intervals continuously, and foot temperatures were recorded for 3 min before and after the footbath and continuously during sleep. DPG was calculated by subtracting abdominal from foot temperature. Paired t-tests were used to compare differences in temperature and sleep variables between the bathing and non-bathing nights.

**Results:** Mean rectal temperature increased 0.1 °C (t = 4.40, p = 0.001) after foot bathing. Mean DPG before lights off was −2.14 °C (SD = 0.57) on the non-bathing night, but was reduced (−0.42 °C, SD = 0.89, t = 6.81, p < 0.001) on the bathing night. The overall amount of REM sleep was increased (t = 2.43, p = 0.03) on the bathing night. There were no significant differences in other PSG sleep variables. However, when NREM cycles were examined separately, sleep efficiency was increased and wake time was decreased (both p = 0.01) in the second NREM cycle, compared to the non-bathing night.

**Conclusions:** A warm footbath provided a sufficient heat load to increase core body and skin temperatures, and REM sleep in older adults with disturbed sleep. Water temperature, timing with respect to sleep onset, and duration of foot bathing are important considerations for future studies of sleep in older adults.

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**Sleep Quality Contributes to Cognitive Performance Differently in Pre- and Postmenopausal Women**

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**Aims:** The purpose of this study was to evaluate the effect of sleep quality on cognitive functioning in pre- and postmenopausal women.

**Methods:** Forty-seven women participated in the study: 20 of them were premenopausal (mean age 48 years) and 27 postmenopausal (mean age 63 years). Cognitive measures included tests of verbal performance, visuomotor functions, short-term memory, episodic memory, auditory attention, shared attention, and controlled processing. Polysomnography was used to assess objective sleep quality and the Basic Nordic Sleep Questionnaire to evaluate subjective sleep quality.

**Results:** Sleep quality and daytime sleepiness affected attention, visual episodic memory, and verbal and visuomotor functions. In premenopausal women the amount of slow wave sleep (SWS) affected cognitive performance more than REM-sleep, whereas in postmenopausal women the effect was opposite. SWS had a slightly negative association with cognitive performance in both groups. On the other hand, in postmenopausal women the amount of REM-sleep correlated positively with performance. Sleep latency and the number of awakenings and arousals had only a minor and inconsistent effect on cognitive functioning, whereas the amount of time awake had a greater and mainly deteriorating influence. In premenopausal women longer time awake was associated with poorer visual episodic memory performance, but in postmenopausal women verbal working memory was affected. Self-assessed daytime sleepiness was associated with poorer cognitive performance. Instead, subjective insomnia had no effect.

**Conclusions:** Poor sleep quality impaired cognitive performance, especially attention, in both pre- and postmenopausal women. The most important finding was the different effect of sleep stages in the two groups. SWS was more important for cognitive performance in premenopausal than postmenopausal women. Because the effect was incongruent it is possible that not only the amount, but also the quality of SWS is essential for cognitive performance in aging women. For instance, analyzing also timing and continuity of SWS may be more sensitive measurement. In postmenopausal women REM-sleep was more significant, which was a novel finding. REM-sleep mainly occurs in the later part of the night. Therefore the amount of REM-sleep may be decreased in women suffering from early awakenings, which may lead to impaired attention.

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**Phase III Study of Ramelteon in a First-Night-Effect Model of Transient Insomnia**

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**Aims:** To evaluate the efficacy of ramelteon, a highly selective MT1/MT2 receptor agonist being studied as a chronosomnotic agent for insomnia treatment.

**Methods:** In this randomized double-blind study, 289 healthy subjects naïve to a sleep laboratory received ramelteon 8 mg, 16 mg, or placebo 30 min before bedtime and underwent overnight polysomnography (PSG). In the morning, a post-sleep questionnaire was completed, and residual effects were assessed.

**Results:** Sleep latency, as measured with PSG, was reduced with ramelteon 8 and 16 mg vs placebo (12.2 and 14.8 vs 19.7 min); the 8 mg dose reached statistical significance (P = 0.004). PSG total sleep time was...
significantly increased with ramelteon 8 mg vs placebo (436.8 vs 419.7 min; P = 0.009) and 16 mg vs placebo (433.1 vs 419.7 min; P = 0.043). Ramelteon had no statistically significant effect on sleep architecture or next-day residual effect measures including Digit Symbol Substitution Test, memory recall tests, and visual analog scales. Adverse event rates were 13.3% for the ramelteon 8 mg group, 6.4% for the 16 mg group, and 12.4% for the placebo group.

Conclusion: Ramelteon promoted sleep in this model of transient insomnia, with no next-day psychomotor, memory, or cognitive effects.

Narcolepsy

O 008
Comorbidity in narcolepsy: prospective data from the narcolepsy register

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Aims: Prospective data is collected in the german narcolepsy register since 2003. Published retrospective data about symptom onset and comorbidity is compared with the prospective data.

Methods: Narcolepsy patients (NP) receive a standardized questionnaire comprising 51 questions prior to hospital admission. On admission a check-list for comorbid diseases and current medication is completed. All NP have a polysomnographic recording, MSLT, HLA typing and in case of given consent a lumbar puncture for assessment of hypocretin. 24 men (mean age 41.9 years) and 32 women (mean age 35.7 years) have been included so far with a mean of 89% of complete data.

Results: Mean age of onset of narcolepsy was 22.5 years. Manifestation of first symptoms showed three peaks as in the retrospective study (20–30, 30–45, 45–60 years), with an onset about ten years earlier in women than in men. The most frequent comorbid diseases were nightmares (41.5%), obesity (34.9%), somniloquy (25.5%), REM behaviour disorder (18.9%), sleep related breathing disorders (SRBD) (17.9%), sleepwalking, headache and periodic leg movement in sleep (PLMD) (each about 14%).

Conclusions: Parasomnias represent the most frequent comorbid diseases, followed by obesity. Narcolepsy and parasomnias have a very high association with HLA DQB1 allele, which might indicate that they share a similar genetic origin. The high frequency of SRBD, which is also quite prevalent in young NP, might be caused by change of muscle tone and obesity. Comorbid diseases may contribute to and earlier diagnosis of narcolepsy.

Respiratory Sleep Disorders

O 009
Rhinological procedures in obstructive sleep apnea syndrome (OSAS)

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Sleep apnea is come to be more and more often diagnosed disease among polish populatin. There are 3 main types of apnea disorders during sleep: central, obstructive and mixed. Obstructive sleep apnea is mainly caused by anatomic changes within the upper airway tract. Diagnosis of OSAS is based on the detection of important apnea disorders during sleep and localization of stenosis within the upper airway tract which are mainly responsible for this disease. Department of Otolaryngology and Laryngological Oncology in Poznan conducts diagnosis and operation treatment of stenosis in upper airway tract in patients with OSAS. One of the most important element of this diagnosis is rhinological procedure based on basic ENT examination, endoscopy, acustic rhinometry and in some cases CT and rhinometry with RhinoSleep. In more than 90% diagnosed patients we found changes in structures of nasal cavities causing poor nasal flow. All patients underwent different operations which improved the nasal flow (plastic operations of septum, conchas, nostrils, osteotomies). Pre- and postoperative examinations revealed that nasal operations are an important part of OSAS treatment, but only in same cases (<10%) they lead to positive termination of treatment.

O 010
Autotitrating CPAP in obstructive sleep apnea (OSA) patients with poor compliance during standard CPAP titration night

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Introduction: Continuous positive airways pressure (CPAP) is considered the standard treatment for the management of OSA patients, but this is often intrusive and poorly accepted by patients. Standard laboratory full polysomnography (PSG) CPAP titration is still considered the gold standard for determining the level of pressure required for each patient. However a proportion of patients remain untreated because of the lack of acceptance to this treatment. Several studies demonstrated that auto-titrating positive airways pressure (APAP) devices improve compliance, comfort and therefore adherence to treatment, with no differences in functional outcomes compared to CPAP.
Aim of the study: to evaluate acceptance and compliance to APAP in a population of OSA patients in which standard manual titration failed and therefore have been considered “untreatable”.

Methods: Two hundred and twenty consecutive severe OSA patients (AHI ≥ 20) referred to our sleep disorders center between January and December 2004 underwent one full-night PSG manual CPAP titration. Based on compliance (time spent with CPAP on), patients were classified as: compliant (C; > 4 hours) and not compliant (NC) including those who were poorly compliant (NC1; between 2 and 4 hours) and those not compliant (NC0; less than 2 hours). The night after manual titration, these NC patients received treatment with APAP (REMSleep® Auto Respiration Inc.).

Results: Characteristics of the whole sample (n=220) were: 187M, 33W; mean age: 53.4 ± 11.5 yrs., Mean Oxygen Desaturation Index (ODI): 42.9 ± 21.9 per hour; minimal SaO2:73.3 ± 10.5.

Thirty-two patients (14.5%; 28M, 4W); mean age: 52.7 ± 14.3 yrs., mean ODI: 48.7 ± 21.4; minimal SaO2: 69.9 ± 10.2 were classified as NC (NC0:n=23; NC1: n=9) and therefore were treated with APAP. Of them, 2 patients showed no compliance also to APAP. Seven patients still had a compliance < 4 hours (mean average use: 2.3 ± 1.1 hours, average pressure: 5.9 ± 1.2 cmH2O; 90th centile pressure: 8.4 ± 1.6 cmH2O) while 23/32 (71.9%) patients showed a good compliance to APAP (mean average use: 6.5 ± 1.6 hours; average pressure: 8.5 ± 1.8 cmH2O; 90th centile pressure: 10.7 ± 2.0 cmH2O).

Conclusion: In this study, the vast majority of patients in which manual CPAP titration failed, precluding eventual treatment, surprisingly showed good compliance to APAP. Our data suggest that APAP should be considered a valid therapeutic alternative in those patients judged “untreatable” with conventional respiratory devices before considering other treatment options (weight loss, ENT surgery etc.).

Reference

O 011
Ambulatory blood pressure monitoring in sleep disordered breathing of various severity
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Aims: Arterial hypertension (H) is one of major under-diagnosed and under-treated cardiovascular complications of sleep disordered breathing (SDB), in spite of its 40–70% prevalence in adults. H can be detected by ambulatory blood pressure monitoring (ABPM) performed mainly for screening and control of anihypertensive therapy.

Methods: More than 20 BP parameters obtained by ABPM were correlated with >30 polysomnographic indices measured in 57 patients with SDB of various severity. They were divided in 4 groups snoring (apnoea/hypopnoea index <5/h, n 12), mild sleep apnoea syndrome-SAS (AHI 5–25/h, n 16), moderate SAS (AHI >25/h, n 17) and a group of severe SAS treated with nasal continuous positive airway pressure (CPAP, n 12).

Results: The time of sleep with snoring correlated with most parameters of diastolic (p<0.05) rather than systolic BP causing a decrease in pulse pressure with increased tissue perfusion. Ventilatory parameters such as snoring, AHI, obstructive apnoea with bradycardia or desaturation, hypopnoea and oxygen desaturation index correlated significantly with an increase (at least p<0.05) in diastolic BP values (nocturnal, diurnal and morning 2 hours, which are most risky for stroke). There was a close negative correlation (at least p<0.05) of minimal and average O2 saturations and SatO2 < 85% with practically all diastolic BPs (morning 2 h, diurnal, nocturnal, minimal) and only with some parameters of systolic BP). CPAP therapy substantially improved both the haemoglobin O2 saturation and BP values by decreasing the number of apnoea/hypopnoea episodes, and eliminating the intermittent hypoxaemia, as well as by decreasing the enhanced sympathoadrenergic activity and frequency of arousal reaction.

Conclusion: ABPM allows to select the most predictive BP parameters for large-scale screening of both the H and SDB, to reveal diastolic H appearing already in early phase of SAS and to manage an effective therapy also for drug-resistant H by long-term use of CPAP treatment.

O 012
Imbalance in pro-inflammatory/anti-inflammatory cytokines in lymphocytes of sleep apnea patients
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Aim: The balance between pro-inflammatory and anti-inflammatory cytokines plays a significant role in atherogenesis. We therefore analyzed the expression of TNF-alpha/IL-10 in obstructive sleep apnea (OSA) patients with and without cardiovascular disorders.

Methods: The cytokine profiles of lymphocytes were analyzed by flow cytometry in 20 OSA patients with hypertension and ischemic heart disease (CVD-OSA) and 23 OSA patients without co-morbidities (only-OSA) matched by AHI and BMI (30.8 ± 13 vs. 30.5 ± 14.2 events/hour and 29.9 ± 13.1 vs. 28.1 ± 4.9 Kg/m²).

Results: Two cytokine profiles were noted. One, which was characterized by high IL-10 and low TNF-alpha expression, was mainly prevalent in only OSA patients (82.6%) as compared to CVA/OSA (49%). In the second,
decreased % of IL-10 and increased % of TNF-alpha expression was predominant in CVD/OSA patients (51%). Notably, a 2-fold increase in the % of TNF-alpha + T cells and a significant decrease in the % of IL-10 + T cells were observed in CVD/OSA compared to only OSA patients. nCPAP treatment significantly lowered the TNF-alpha expression in both patient groups and thus ameliorated the TNF-alpha/IL-10 imbalance expressed in T cells.

Conclusion: OSA patients with T cells expressing low IL-10/high TNF-alpha may be at a higher risk of cardiovascular morbidity. Therefore the diagnosis at the cellular level may help to identify these patients at risk.

O 013
The craniofacial morphology and sleep disordered breathing in children with nasal obstruction

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Children with nasal obstruction may sleep undisturbed or suffer from different degrees of sleep disordered breathing, ranging from snoring to severe obstructive sleep apnea. Young patients with sleep-disordered breathing are usually cured if nasal obstruction is resolved by adenoidectomy. The aim of our study was to find out whether anatomical or functional factors are responsible for the different upper respiratory tract behaviour, and if anatomic factors exist, to isolate and to define the features which predispose to the development of sleep disordered breathing in the presence of nasal obstruction. Forty-four consecutive children, 23 boys and 21 girls aged 3 to 16 years with nasal obstruction and without tonsillar hypertrophy, known craniofacial anomalies or neuromuscular diseases were included in the study. Relying on parents’ report and on medical history, a differentiation was made between the patients with rest sleep and those with varying severity of sleep disordered breathing. Cephalometric measurements used for assessment of craniofacial features were correlated with the clinical evaluation. A direct correlation was found between anatomy and sleep breathing patterns. Increased tongue volume, dorsocaudal location of the hyoid bone, obtuse gonial angle with retruded mandible and decreased flexure of the cranial base are the four morphological deviations that characterize patients prone to develop sleep disordered breathing. Some abnormalities of facial skeleton have been influenced by age, deteriorating as the child continued to be a chronic mouth breather, and are similar to those found in many adult snorers. In conclusion, sleep disordered breathing in children with nasal obstruction is of anatomical rather than functional origin. Chronic mouth breathing during the growing process has detrimental effects on the dentofacial development, leading to craniofacial deformities, which are also a significant contributing factor to the underlying aetiology of adult OSA. Surgical correction of persistent nasal obstruction early in life is mandatory even if in most cases, the original cause will spontaneously be resolved.

O 014
Sleep-Disordered Breathing Surgery in Outpatient Setting: Personal Experience and Results

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Aims: Retrospective evaluation of radiofrequency volume reduction (RFVR) mini invasive surgical technique applied in sleep disorder breathing surgery (SDBS).

Methods: In our ENT Unit, from February 2000 to April 2005, we performed RFVR on 108 SDBS patients (pts) (simple snoring and slight Obstructive Sleep Apnea Syndrome): 71 as first surgical procedure and 37 as second surgical procedure, after a first phase of SDBS surgery with not completely resolution of snoring. All the procedures have been made with radiofrequency generator and electrical device by “Somnus”® and “Celon”®. We treated 57 soft palate (SP), 1 uvula (U), 2 adenoids (A), 44 turbinates (TU), 22 tongue base (TB), 5 tonsils (T) and 5 genio-glossus muscle (GGM). We performed all surgical procedures under local anesthesia in outpatient setting.

Results: Disappearance of snoring was observed in 76.2% of the 71 primary pts and in 85% of the 37 revision pts.

Conclusions: The RFVR is an effective technique for snoring reduction with high compliance of patients and low pain in the post-operative time.

O 015
Itamar®System as Practical Tool for Sleep Study in Ent Clinic: Preliminary Results

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Aims: Retrospective evaluation of the new Watch-PAT 100®, an ambulatory unattended diagnostic device for the sleep-disordered breathing diseases (SDBD). This
device uses the zzzPAT software of the second generation. We realized the study in comparison with POLYMESAM®.

Methods: The WP100 measures the PAT (Peripheral Arterial Tone) signal utilizing a plethysmographic-based finger-mounted probe. The PAT signal reflects the pulsatile volume changes in the fingertip arteries, that is correlated with the arterial vasomotor activity and indirectly the level of sympathetic activation. These measures could be correlated with the sleep phases. These characteristics of Watch-PAT 100 system allows the detection of respiratory events, differentiation between wakefulness and sleep, arousals from sleep and the differentiation between sleep and REM sleep periods. We used the WP100 in 15 patients with (SDBD) from simple snoring to severe OSAS comparing WP100 data with POLYMESAM data.

Results: the RDI measured with the Watch-PAT 100 is comparable with the other system, with score difference ≤2.

Conclusions: the WP100 is practical device with a good compliance for the patient and results are comparable with other unattended sleep PSG systems.

O 016
Respiratory Failure in Obstructive Sleep Apnea Syndrome (OSAS)—Is CPAP Therapy Alone Adequate?

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Aim: To assess the efficacy of long-term nocturnal continuous positive airway pressure (CPAP) treatment in 11 hypercapnic (daytime pCO₂ > 45 mmHg) obstructive sleep apnea syndrome (OSAS) patients we repeated BMI, spirometry and arterial blood gases (pCO₂ and pO₂) data before and after 6 months of treatment. Concomitant lung and thyroid disease were excluded. The mean apnea index before therapy was 56.8 events/hour. Compliance of CPAP use of 5 hours/night or more was required.

Results: BMI (36.0 ± 3.6 to 34.7 ± 3.6 kg/m²; p = NS) and spirometry data (FEV1 80.5 ± 9.3 to 76 ± 14.0; p = NS) did not change significantly after therapy. pCO₂ decreased to normal values (50.2 ± 4.5 to 40.6 ± 2.2 mmHg; p < 0.0001), and pO₂ increased significantly (56.3 ± 6.0 to 64.5 ± 6.0 mmHg; p = 0.005) with CPAP. No significant change in secondary erythrocytosis was observed (169.7 ± 31.7 to 161.0 ± 13.1; p = NS).

Conclusion: These results indicate that in severe OSAS mild hypercapnia can be normalized by CPAP therapy alone (since patients remained equally obese). This further implies that abnormal ventilatory drive in OSAS can be successfully reversed.

O 017
Relations between body mass index, lung function and respiratory disturbance index in obese males with obstructive sleep apnoea syndrome

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The relation of mortality to respiratory disturbance index (RDI) or body mass index (BMI) has recently been published as far as males with sleep apnoea syndrome are concerned (Eur Respir J 2005, 25, 514–520). The aim of this study was to find out if there is any correlation between BMI, lung function and RDI in 30 obese males (mean age 57, range 27–74 years, mean height 177, range 168–189 cm, mean weight 105, range 73–146 kg) with obstructive sleep apnoea syndrome.

The BMI (X ± SD) was 34 ± 6 kg/m², RDI 39 ± 24, oxygen saturation (SAT) 76 ± 10%, forced expiratory vital capacity (FVC) 86 ± 13% (predicted) and forced expiratory volume in 1 second (FEV1) 85 ± 23% (predicted).

Significant correlations (R) were found between height vs. weight (R = 0.56, p < 0.01), BMI vs. weight (R = 0.92, p < 0.001), BMI vs. SAT (R = −0.48, p < 0.01), RDI vs. SAT (R = −0.44, p < 0.02), RDI vs. weight (R = 0.37, p < 0.05), FVC vs. weight (R = −0.45, p < 0.02), and FVC vs. FEV1 (R = 0.57, p < 0.01). No significant relation could be detected between BMI and RDI (R = 0.33).

This study shows that the investigated obese males had no signs of any obstructive or restrictive ventilation disturbances. The RDI was only significantly related to oxygen saturation and body weight and showed no significant correlations to the lung function parameters. The lack of a correlation between BMI and RDI let suppose that the appropriate parameter for the estimation of the severity of an obstructive sleep apnoea syndrome is not the BMI but the body weight.

O 018
Reduction of sleep apnea after the orally available cholinesterase inhibitor donepezil

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Study objective: To extend previous findings that the cholinesterase inhibitor (CEI) physostigmine, by continuous infusion, reduces Apnea/hypopnea Index (AHI) predominantly during REM sleep in patients with obstructive sleep apnea (OSA).
**Introduction**: Patients with obstructive sleep apnea (OSAS) have an increased accident risk. In patients with OSAS and daytime sleepiness the German Society of Sleep Research and Sleep Medicine (DGSM) recommends that driving abilities should be re-established 6 weeks after CPAP-initiation and documentation of therapeutic effects on daytime symptoms and performance. This period is too long especially with regard to socioeconomic consequences and possible sanctions for the drivers like e.g. unemployment. The present study was conducted in order to investigate whether an improvement of driving abilities can be documented in a simulated driving situation 14 days after initiation of CPAP which might justify an earlier return to driving e.g. in commercial drivers.

**Patients and Methods**: Driving simulation and neuropsychological testing of vigilance were conducted in 36 patients with OSAS before and 2 (n=23), 14 (n=18) and 42 days (n=17) after initiation of CPAP. Results: Vigilance testing showed only slight changes under CPAP. Frequency of accidents during driving simulation was reduced after 14 days of CPAP, however a significant decrease was achieved only on day 42. In contrast, concentration faults were significantly reduced after 2 and 14 days of CPAP.

**Conclusions**: In OSAS-patients with documented improvement of daytime performance (e.g. 2 weeks after initiation of CPAP) especially in professional drivers driving permission may be granted earlier than the recommended 6-weeks-period.

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**O 019**

**Driving simulation and neuropsychological testing in patients with OSAS-legal consequences?**

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**University Hospital Bergmannsheil, ¹Division of Pneumology, Allergology and Sleep Medicine, ²Division of Neurology, Bochum**

**Design**: Randomized, double-blind, parallel group trial comparing the orally available CEI donepezil (Aricept, 5 mg o.d.) and placebo on polysomnography and questionnaire (minor symptom evaluation, MSE) based outcomes. Evaluations were made at baseline and at 21 days.

**Participants**: In total 40 patients with moderate to severe OSA (mean age 52.3 years, mean BMI 28.0 kg/m², mean AHI on previous screening 30.4 events/h). Thirty eight patients (18 on placebo and 20 on donepezil) completed both study nights.

**Interventions**: Donepezil (Aricept, 5 mg o.d.) or corresponding placebo.

**Measurements and Results**: Donepezil did not affect SWS but increased REM sleep percentage from 12.9 (3.2) to 17.3 (5.4) %. Total sleep time (361 (41) and 367 (53) min., respectively) was unchanged. The main finding was a 31% reduction of AHI from 35.6 (23.0) to 24.4 (14.8) (p<0.035 vs. placebo) and a 60% reduction of AI during REM sleep from 16.1 (20.5) to 6.4 (11.8) (p<0.018 vs. placebo). OSA indices remained essentially unchanged during non-REM sleep. The overall (non-REM plus REM) AHI and apnea index (AI) were marginally reduced in the donepezil group (36.9 (22.8) to 34.7 (25.4) and 17.6 (19.6) to 13.7 (14.3). Sleep time, sleep stages and severity of OSA were all unchanged in the placebo group. The effect on hypopneas in either group was small. In contrast, hypoxic episodes appeared to be more prominently attenuated after donepezil as indicated by an increase in mean minimum overnight oxygen saturation from 69.4 (18.3) to 74.4 (18.3). A post-hoc analysis (unadjusted linear correlation) suggested that lower body mass index (BMI) and lower heart rate at base line were associated with a stronger REM-AI treatment response. Subjective daytime symptom load as evaluated by the MSE scale revealed improvements in the dimensions contentment (8 items, p<0.013), general well-being (p<0.03) and total MSE score (24 items, p<0.12) after donepezil compared with placebo.

**Conclusions**: The orally available CEI donepezil exerts a beneficial effect on apneic episodes during REM sleep. The finding corroborates our earlier findings on the CEI physostigmine and suggests a specific pharmacological effect of this drug class in OSA. This effect may potentially be increased by additional patient stratification in future trials.

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**O 020**

**Morbidity in moderate-severe obstructive sleep apnoea before and after CPAP treatment**

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**Department of Sleep Medicine, University Hospital Glostrup, COWI A/S, and Center for Health Technology Assessment, National board of Health, Denmark**

Sleep apnoea is associated with social consequences, traffic accidents, morbidity and mortality. CPAP is the best documented treatment for moderate-severe sleep apnoea. It is still debated whether chronic CPAP treatment reduces morbidity.

**Aim**: to evaluate whether chronic CPAP treatment reduces morbidity as compared to pre-treatment morbidity.

**Methods**: 137 consecutive patients in who CPAP treatment were initialized in the period 2000–2001 were enrolled. Morbidity evaluated from The Danish National Patient Registry in which all contact including primary and secondary health contacts are registered by procedures and diagnosis. Registration of all contacts two year prior and after CPAP treatment was compared. Furthermore comparisons were made to age- and gender-matched controls.
Results: Patients with moderate-severe sleep apnoea (AHI exceeding 15 per hour) presented double as high number of health contacts from all diagnoses and cardio- and cerebrovascular diagnosis in both the primary and secondary health sector as compared to an age- and gender-matched Danish background population. CPAP treatment significantly reduced these contact but not to the level of the background population. The morbidity reduction was more pronounced two years after start of CPAP treatment than during the first year of contacts.

Conclusion: patients with moderate-severe obstructive sleep apnoea present significantly higher morbidity, including cardio- and cerebrovascular morbidity, compared to the background population. The morbidity is reduced by CPAP treatment.

O 021
Health Technology Assessment in Sleep Apnoea

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Sleep apnoea is associated with social consequences, traffic accidents, morbidity and mortality. Diagnosis and treatment are performed in different settings and methods. In-hospital supervised polysomnography (sPSG) is accepted as best available methods for diagnosing sleep apnoea. Due to the prevalence of sleep apnoea, a general use of sPSG for diagnosing sleep apnoea has major implication for the organization and health economy as sPSG is staff demanding and expensive. Other methods like respiratory polygraphy (RP) and oximetri (Ox) have been suggested as alternative methods.

Aim: (1) to evaluate the best methods for diagnosis of sleep apnoea, (2) to evaluate the best treatment methods, and (3) evaluate the economical consequences of implementation of three scenarios in diagnosing and treating sleep apnoea: (a) sPSG, (b) ambulatory RP, and (c) ambulatory Ox. All scenarios followed by CPAP treatment in patients identified with moderate-severe sleep apnoea.

Methods: (1) A systematic review of the literature regarding diagnosis and treatment of sleep apnoea. (2) A health economical analysis of the three scenarios, including morbidity data from a 2 year before and 2 year after CPAP treatment (The Danish National Patient Registry) including 137 patients with moderate-severe sleep apnoea compared to the Danish population. Sensitivity and specificity of each scenario, and for economical estimates diagnose related groups (case-mix), equipments, depreciation, staff etc were included in the model.

Results: (1) Sensitivity and specificity of partial respiratory polygraphy was moderate-good, varying between 82–94% and 82–100%, respectively. The sensitivity and specificity of oximetri was poor-moderate varying between 35–100% and 23–100%, respectively. (2) CPAP is the best documented treatment for sleep apnoea. Treatment effect of auto-adjusted and fixed pressure CPAP are similar, but auto-CPAP may present organizational advantages. (3) SPSG is expensive, consequently the number of patients who may be diagnosed and treated is limited as compared to partial respiratory polygraphy. Oximetri offers no economical advantages compared to partial respiratory polygraphy. (4) Treatment of sleep apnoea in ambulatory settings is cost-effective.

Conclusion: Despite RP present lower diagnostic yield than sPSG in the diagnosis of uncomplicated sleep apnoea, implementation of RP will imply that more patients can be diagnosed and treated, than if supervised polysomnography is used, for the same economical resources. The disadvantages are that some patients are misdiagnosed and not treated. Ox offers no diagnostic or health economical advantages and cannot be recommended for the primary diagnosis. Diagnosing and treatment with CPAP of sleep apnoea is cost-effective, even if only morbidity-data are included. Future health related economical analysis should include social, professional and traffic aspects.

O 022
Neuropsychological Changes after Sleep Disordered Breathing Surgery in OSHAS

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Aims: Investigation of neuropsychological performances in 100 OSAHS patients before and after surgery

Methods: 100 OSAHS patients (mean RDI 32.4, SAO2 79.2) compared to 100 age-matched normal controls before and six months after surgery. The psychological battery were performed at PT and PO: (1) Epworth Sleepiness Scale (E.S.S.); (2) Center for Epidemiological Studies Depression Scale (CES-D); (3) Perceived Stress Questionnaire (PSQ); (4) Illness Behaviour Questionnaire (IBQ); (5) PC assisted neuropsychological testing for vigilance, visual and uditive alertness, selective attention; (6) A questionnaire for self-perception of symptoms (sleepiness, work performances, attention, concentration, manual dexterity, social problems, family’s problems, sexual difficulties), stimulants consumption (cigarettes, coffee, the, coca cola), accidents in the last six months.

Results: A significant improvement in EDS (ESS: p<0.001), depression (p<0.0001), perceived stress (PSQ p=0.111), vigilance (p=0.0023), lective attention (p<0.0001), daily cigarettes and coffee, self-perceived manual dexterity (p<0.0001), social problems (p<0.0001), family’s problems (p<0.0001), sexual difficulties (p<0.0001).
Conclusion: surgical treatment seems to improve some neuropsychological performances and psychological variables, compared to controls.

O 023
Previously undiagnosed obstructive sleep apnea in patients with HyperCKemia and the effects of CPAP treatment

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Study objectives: To evaluate the impact of obstructive sleep apnea syndrome (OSAS) on serum creatine phosphokinase (CK).

Methods: Single centre prospective cross-sectional study of 201 consecutive patients (age = 54.9 ± 11.0 years, 155 males/46 females, BMI = 31.3 ± 6.9 kg/m²) with suspected sleep-disordered breathing.

Results: Sixty-seven patients (38%) showed an asymptomatic and unexplained CK elevation. OSAS was confirmed in 182 patients (apnoea/hypopnoea index [AHI] > 5/h) and ruled out in 19 patients (controls) by standard polysomnography. Baseline CK was significantly higher in severe OSAHS (AHI > 30/h, n = 89) compared to mild-to-moderate OSAHS (AHI = 5–30/h, n = 93) and controls (191.4 ± 12.9 U/l vs. 134.3 ± 7.5 U/l vs. 107.1 ± 7.9 U/l, p < 0.01). Receiver operating curve analysis identified an optimal cut-off value of > 148 U/l (R = 0.660) for CK, which yielded a positive predictive value of 99%, a sensitivity of 43%, and a specificity of 95% for the diagnosis of OSAS. Mean nocturnal oxyhemoglobin saturation was the main predictor of CK (R = 0.45, p < 0.001). Continuous positive airway pressure (CPAP) treatment resulted in a significant decline of CK both in mild-to-moderate (n = 38, 129.7 ± 13.4 U/l vs. 96.7 ± 7.6 U/l, p < 0.001) and in severe OSAS (n = 39, 187.7 ± 18.9 U/l vs. 132.2 ± 12.9 U/l, p < 0.001).

Conclusions: Up to one-third of OSAS patients showed a CK elevation that was partly reversible with CPAP treatment. OSAS may account for a substantial number of cases of unexplained CK elevation (HyperCKemia). We therefore propose further studies to address the prevalence of OSAS in patients with mild to moderate hyperCKemia.

O 024
Influence of nasal resistance on CPAP pressure

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Introduction: Patients with severe sleep apnea were treated with CPAP therapy. The application of the pressure takes place via a nasal mask. Nasal complaints were often notices after start of CPAP therapy as well as during longterm therapy. Nasal flow below 180 ml/s on one side or flow reduction on both side below 500 ml/s were described as limitation. The aim of this study was to examine the connection between CPAP pressure and nasal resistance.

Methods: 80 Patienten with severe OSAS were examined (AHI 38/h, BMI 30.8 kg/m²). Every patient got anterior rhinomanometria before CPAP therapy was started. From these data we derived the flow of each nasal side and the flow through both sides to evaluate the nasal breathing.

Results: The nasal flow on one side was on average 242 ml/s (range 84–600 ml/s), the flow of both sides together was on average 734 ml/s (range 352–1134 ml/s) (group A + B). 17 patients had a limited flow in one or both nasal sides (group A). 11 patients (6 with reduced flow) needed a heated humidifier to continue CPAP therapy after the first night because of nasal complaints.

After 30 minutes CPAP therapy during the day no patient had a reduction of nasal flow.

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>A + B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>17</td>
<td>63</td>
<td>80</td>
</tr>
<tr>
<td>Flow on one side in ml/s</td>
<td>155</td>
<td>272</td>
<td>242</td>
</tr>
<tr>
<td>Flow on both sides in ml/s</td>
<td>325</td>
<td>801</td>
<td>734</td>
</tr>
<tr>
<td>Number of humidifier</td>
<td>6</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>CPAP pressure in mbar</td>
<td>7.5</td>
<td>8.1</td>
<td>7.7</td>
</tr>
</tbody>
</table>

Discussion: Data showed there is no connection between CPAP pressure and nasal resistance. Nasal complaints depend on integrity of mucous membranes and the endonasal distribution of the air. Therefore rhinomanometria can only be an additional tool to find patients with endonasal abnormalities and treat them accordingly.

O 025
Prevalence of symptoms of disordered breathing during sleep in rural Delhi, India

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Aim: To determine the prevalence of symptoms associated with disordered breathing during sleep in adults residing in rural Delhi, India so as to raise the awareness level about this health problem.

Patients and Methods: A total of 19 villages were randomly selected from 232 villages of Delhi. Households from each village were then selected randomly to obtain a sample of 350–400 subjects. The study was done using a questionnaire consisting of 15 multiple-choice questions. The field investigators made house-to-house visits and...
administered the questionnaire to all individuals over 18 years of age. A repeat visit was made by the investigators to contact the members who were absent during the first visit. Each question was scored depending on the severity of symptoms.

**Results:** A total of 7016 questionnaires were filled. Snoring in 6.9% of the sample, was the most common symptom of sleep-related breathing disorders and was significantly associated with male sex, age more than 19 years, obesity, diabetes mellitus, hypertension, nightmares and sweating during sleep, early morning awakenings (with difficulty in resumption of sleep) and mood changes. Daytime sleepiness, the other most common symptom was reported by 2.6% of the subjects and was significantly associated with breathing pauses during sleep, diabetes mellitus, memory lapses and tiredness during daytime. Only 0.6% of individuals gave a history of breathing pauses during sleep.

**Conclusions:** Disordered breathing during sleep is as yet an undiagnosed entity in India. Doctors should ask patients and bed partners regularly about clinical features like snoring and daytime sleepiness.

**O 026**

**Pilot Testing of Cost Effective Approach to Screening, Diagnosis, Treatment of Sleep Apnea in Commercial Motor Carriers**

Moscovitch A.1, Reimer M.1, Rhodes W.2, Heslegrave R.3, Hirshkowitz M.4

1Canadian Sleep Institute #300, Calgary, Canada; 2Rhodes & Associates Inc., Toronto, Canada; 3Psychiatry, University Health Network, University of Toronto, Canada; 4Sleep Disorders and Research Centre, VAMC Sleep Centre, Baylor University, Dallas, USA

**Objectives:** Sleep apnea is becoming an emerging concern in the transportation sector, and a key clinical cause contributing to operators’ fatigue. This abstract outlines the development and successful field operational testing of a step-wise, cost effective and practical approach for screening, diagnosis and timely treatment of this condition, as part of a comprehensive fatigue management program.

**Methods:** Twenty-nine (29) Alberta and Texas drivers completed subjective screening (multi-variant apnea index-map) EPWORTH sleepiness scale, Sleep Apnea Quality of Life Index (SAQLI) and two levels of objective ambulatory screening, utilizing the sleep strip and Eden-trace II. All drivers with an RDI ≥15 were seen subsequently for clinical consultation within 72 hours, and underwent polysomnography with subsequent treatment, as required.

**Results:** In this sample, 72% had at least a mild degree of sleep apnea, with 41% warranting intervention and treatment. The sequential approach utilizing ambulatory screening accurately predicted the conditions in 82% of tested participants, with no false negatives noted. Of the drivers diagnosed with the condition in Alberta, 78% improvement was noted in sleep time, with an increase from mean sleep of 3.9 hours to 6.8 hours on work days. This stepwise, cost effective approach to screening and diagnosing of this condition in operational environment has been successfully pilot tested with good reception by participating operators, timely access to treatment and intervention when required, and no interference with the individuals work schedule and driving ability.

**Conclusion:** As expected, treatment of this condition resulted in most significant improvement in sleep and fatigue parameters.

**O 027**

**North American Pilot Fatigue Management Program (FMP) for Commercial Motor Carriers (Alberta Results)**

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1Canadian Sleep Institute #300, Calgary, Canada; 2Rhodes & Associates Inc., Toronto, Canada; 3Psychiatry, University Health Network, University of Toronto, Canada; 4Sleep Disorders and Research Centre, VAMC Sleep Centre, Baylor University, Dallas, USA

**Objectives:** This presentation outlines the results of a unique, comprehensive Fatigue Management Pilot Study for the motor carrier industry. Piloted in Alberta, it was adopted for further testing in two additional jurisdictions (Quebec and Texas).

**Methods:** The FMP consisted of customized educational, operational and clinical sleep disorder intervention, conducted with drivers on revenue generating routes. Data collection methods were structured to ensure minimal interference to drivers and companies. Pre- and post- data collection, involved subjectively and objectively measuring sleep and fatigue (actigraphy and PVT). Data was collected from four commercial motor carriers in Alberta (three trucking and one busing company) with continuous incorporation of participants’ feedback.

**Results:** Sample survey results indicated close to 60% of drivers needed at least 7 hours of sleep, with 71% chronically getting less; 84% reported fatigue-related mistakes or mental errors several times a year; 26% reported nodding off or falling asleep while driving. Comparative analysis showed drivers significantly over estimated total sleep time on work and off-days. At commencement, mean work days sleep time was 304 minutes and mean off duty sleep just slightly longer (<6 hours). 71% had at least a mild degree of sleep apena; 38% warranted treatment. Fatigue and sleep measurements
improved significantly following pilot implementation; sleep time increased 73% in drivers treated for sleep apnea.

**Conclusion:** Previous studies subjectively assessed fatigue problems in commercial drivers or objectively measured the problem scope. The uniqueness of this study resulted in a customized comprehensive intervention model, which addressed the problem and delivered scientific measurements upon which to base a future large scale field operational test.

### O 028

**Improvement of CPAP-therapy by C-Flex?**

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**Introduction:** It has been noted that the conservative CPAP therapy is frequently accompanied by respiratory complaints, which affects the goals of breathing therapy. During C-Flex therapy the patient’s breathing is continuously monitored to reduce respiratory complaints. We wanted to address the question if a more comfortable treatment of OSAS (obstructive sleep apnea syndrome) can be achieved by C-Flex when compared to CPAP.

**Methods:** Sixty patients with severe OSAS have been examined (ages 52.4 ± 12.5 years, body mass index 39 ± 16 kg/m², AHI 44 ± 12/h). There were divided into two groups and either treated with CPAP (30) or C-Flex (30). The patients’ individual states of health were determined by questionnaire. The results from 12 months of therapy were as follows.

**Results:**

<table>
<thead>
<tr>
<th></th>
<th>Prior to CPAP</th>
<th>after 12 month</th>
<th>Prior to C-Flex</th>
<th>C-Flex after 12 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESS</td>
<td>13.4 ± 2.9</td>
<td>5.1 ± 2.9</td>
<td>14.6 ± 4.9</td>
<td>5.8 ± 4.7</td>
</tr>
<tr>
<td>AHI n/h</td>
<td>44 ± 12</td>
<td>3.2 ± 1.4</td>
<td>48 ± 15</td>
<td>2.3 ± 6.1</td>
</tr>
<tr>
<td>Pressure in mbar</td>
<td>10.3 ± 1.9</td>
<td>9.8 ± 2.7</td>
<td>87 ± 12</td>
<td>85 ± 7.8</td>
</tr>
<tr>
<td>% days with therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average use in h/d</td>
<td>5.7 ± 1.8</td>
<td>5.5 ± 2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Side effects (mask)</td>
<td>10 Pat. (33%)</td>
<td>9 Pat. (30%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Side effects (instrument)</td>
<td>5 Pat. (16%)</td>
<td>3 Pat. (10%)</td>
<td></td>
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**Discussion:** C-Flex is an augmentation in OSAS therapy. Twelve months of observed therapy indicate no difference in the length of use and compliance between C-Flex and CPAP. However, the C-Flex group showed a trend towards reduced side-effects. To what extent that indicates a lasting improvement in the compliance is still to be determined.

### O 029

**Prevalence of obstructive sleep apnoea (OSA) in males and females: epidemiological study vs sleep lab data**

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Results of recent population studies suggest that sleep related breathing disorders (SRBD) are more frequent in females than previously estimated.

The aim of this study was to evaluate male to female ratio in the diagnosis of OSA comparing results of an epidemiological study on SDRB in Warsaw with data from a Sleep Laboratory. Epidemiological study During investigations of by overnight PSG in a representative population sample of Warsaw (676 subjects; 320 females and 356 males), mean age 56.6 ± 8.2 years (range 41–72), OSA was diagnosed in 76 subjects (11.3%). Diagnosis of OSA was 3-times higher in males (59; 16.7%) than in females (17; 5.4%) (p < 0.001). Females with confirmed OSA were not significantly older and more obese (62.6 ± 6 years and 32.3 ± 6 kg/m²) than males (59 ± 7.7 years and 30.2 ± 4.9 kg/m²). Severity of OSA in both sexes was similar (AHI/RDI – 25.2 ± 15.2 and 25.4 ± 16.4, mean SaO₂ – 92.2 ± 3.3% and 92 ± 3.3%, respectively in females and males). Females spent more time in desaturation below 90% (T90) – 26.9 ± 34% when compared to males (16.6 ± 19, 9%) (NS). Sleep lab. data In 3785 subjects evaluated at our Sleep Laboratory, OSA was confirmed in 1657 (43.8%). Diagnosis of OSA was 6-times higher in males (1426 subjects; 86.1%) than in females (231 subjects; 13.9%) (p < 0.001). Females with confirmed OSA were significantly older (57.8 ± 9.9 years) than males (51.9 ± 10.4 years; p < 0.001). BMI was slightly higher in females – 33.6 ± 7.6 kg/m² comparing to males – 32.8 ± 6.2 kg/m² (NS). Males presented more severe OSA – AHI/RDI - 43.2 ± 24.5 than females -AHI/RDI - 38 ± 24 (p = 0.035). However, females had lower mean SaO₂ and longer time T90 than males [mean SaO₂ – 88.2 ± 7.2% and 89.1 ± 7% (NS), T90 – 26.9 ± 34% and 16,6 ± 19,9% (NS) respectively in females and males]. In conclusion, predominance of OSA diagnosis in males was twice more higher in subjects referred to Sleep Lab for SRBD than one could expect from an epidemiological study.

### O 030

**A Double Blind, Cross-over Placebo Study of the use of Sildenafil in Severe Obstructive Sleep Apnea**

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Objective: To determine the effect of Sildenafil 50 mg on sleep and cardiovascular parameters in severe Sleep Apnea Hypopnea Syndrome (OSAHS).

Methods: Fourteen men with severe OSAHS (IAH > 30/h) were consecutively selected. Mean ± SD age was 60.4 ± 10.9 years and mean ± SD BMI, 35.4 ± 8.4 Kg/m². Exclusion criteria: cardiovascular and/or chronic respiratory disease. All-night polysomnography (PSG) was recorded (Harmonic™, Stellate System) immediately after receiving a single dose of Sildenafil 50 mg or placebo. Autonomous nervous system activity was assessed by heart rate variability (Somnologica™, Embla) on the EDF recording and arterial pressure (AP) by BeatScope 1.0™ (TNO) were simultaneously performed.

Results: After the use of Sildenafil 50 mg, % of sleep time with Sat O₂ < 90% (14.2 ± 9.1 vs 8.5 ± 3.2%, p < 0.05) increased, but no difference between groups was observed neither on the nadir of O₂ desaturation, nor on the duration of the apnea-hypopnea events. Increase in mean RR intervals (702 ± 119 vs 907 ± 113 ms, p = 0.05) and in rMSSD (45 ± 23 vs 30 ± 9, p < 0.05), as well as decrease in mean and diastolic AP were also observed (93 ± 12 vs 85 ± 13, and 72 ± 9 vs 67 ± 18 mm Hg, respectively, p < 0.05, both).

Conclusion: In OSAHS, despite the increase in time with Sat O₂ < 90 mm Hg after the use of Sildenafil, which may be attributed to a shunt effect, no decrease in the nadir O₂ desaturation occurred. The decrease in diastolic AP (vasodilatation effect), and increase in mean RR intervals and in rMSSD suggest parasympathetic activation after pre-sleep use of Sildenafil.

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O 031
A Novel Appliance for Treatment of Obstructive Sleep Apnea using Continuous Positive Airway Pressure

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Aims: For patients suffering Obstructive Sleep Apnea (OSA) the efficacy of cpap treatment is undisputed. It is also widely accepted that a large fraction of patients do not tolerate the nasal or full-face masks necessary for successful cpap treatment. Moreover many patients who do accept these masks suffer side effects ranging from skin and nerve irritation to severe pressure ulceration due to imperfect fit of the masks. Much effort is put into reducing the mask size and improving the fit, but the fundamental problems of an appliance placed onto the nose and mouth remain mostly unchanged.

Methods: A new approach which does away with most of these shortcomings has been developed and is currently under evaluation. The basic idea is to use an individually made mouthpiece that fits precisely into the oral vestibulum. This mouthpiece is then connected to the air supply hose of the cpap system. No part of the mouthpiece protrudes through the dental arch thus no bite lock occurs. Only a small anatomically shaped conduit protrudes though the lips to connect to the air hose. The shape of this mouthpiece is chosen for maximum extension without inhibiting the closure of the mouth and without significantly displacing any soft tissue. The design follows the idea of Fränkel who was the first to use muscular tension to generate useful forces with appliances placed entirely in the oral vestibulum.

Results: The design principle of the new individual mouthpiece will be shown together with the fabrication procedure. First clinical experience will be presented.

Conclusions: It is possible to successfully apply cpap treatment to patients who rejected the conventional mask. The side effects of the treatment can be drastically reduced and thus the compliance can be expected to increase by a huge margin.

O 032
Cerebrovascular surrogate markers in sleep apnea

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Aim: There is increasing evidence of a causal interaction between obstructive sleep apnea (OSA) and cerebrovascular disease. The aim of the study was to elucidate the relationship between the polysomnographically (PSG) measured severity of OSA and carotid atherosclerosis determined by ultrasonography and serum surrogate markers.

Methods: 147 patients (102 males, 45 females), referred to our sleep laboratory for evaluation of snoring and sleep-disordered breathing were investigated. Carotid atherosclerosis was evaluated by serum analysis of high-sensitivity C-reactive protein (hs-CRP) and fibrinogen and four sonographic indices: intima-media thickness (IMT) of the common carotid artery (CCA), bulb to internal carotid artery (Bulb-ICA), combined IMT measurements from all segments and a plaque score (PlaS). Pearson correlation analysis, intergroup comparison (ANOVA), covariance analysis and a multiple regression were performed to assess the association between surrogate markers and respiratory variables.

Results: 44 patients had no OSA (apnea-hypopnea index AHI < 5/h), 27 mild (AHI 5–15), 27 moderate (AHI 15–30) and 51 severe OSA (AHI > 30). After adjusting for potential
confounders, significant differences between the controls and all three OSA groups were observed in the CCA-IMT (p=0.032) and in the PlaS between the controls and the severe group (p=0.034). Multiple regression revealed the AHI as an independent predictor of CCA-IMT (p=0.001) and combined IMT (p=0.001), whereas the percentage of total sleep time with an oxygen saturation below 90% was associated with Bulb-ICA IMT (p=0.018) and hs-CRP (p=0.015).

Conclusion: OSA is associated with higher surrogate levels of cerebrovascular disease. Even mild OSA seems to predispose to early atherosclerosis.

O 033
Diagnosis of obstructive sleep apnoea and hypopnoea syndrome based on automatic analysis of mandibular movements

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Aims: The mandibular movements have been shown to be correlated with the oesophageal pressure during episodes of sleep apnoea and hypopnoea. Our study highlighted the potential of an automatic analysis of mandibular movements for the diagnosis of obstructive sleep apnoea and hypopnoea syndrome (OSAHS) by the measurement of the apnoea and hypopnoea index (AHI).

Methods: Twenty-four middle-aged patients with OSAHS (AHI: 33.7±30.7) were considered in our study. For each patient, a full polysomnography (PSG) was recorded in hospital settings, mandibular movements were recorded synchronously with the other channels. The jaw motion was also recorded previously to the PSG for fifteen patients, at home with an ambulatory device. Standard rules about the definition of apnoea, hypopnoea and sleep stages were applied to compute the AHI from the PSG, called AHI_PSG. The automatic analysis of mandibular movements was performed to get the automatic AHI for both recordings, respectively AHI_A (ambulatory) and AHI_H (hospital). The automatic analysis was based on the detection of salient jaw motions occurring after apnoeas and also on the analysis of jaw motions related to breathing efforts. AHI_PSG, AHI_H and AHI_A were compared with each other to measure the accuracy, the reliability and the correlation of our automatic method with the gold standard.

Results: To measure the accuracy of the diagnosis, sensitivity and specificity were computed from AHI_A and AHI_PSG for different values of an acceptance threshold. The two most interesting cut-off on AHI were 11 and 19: sensitivity was respectively 90% and 100%, specificity was 100% and 88.9%. The linear regression (slope p=0.99) and the correlation coefficient (r=0.98) between AHI_A and AHI_H revealed good reliability of our method. The Bland and Altman plot of the differences (AHI_A-AHI_H) showed a mean of −2.1±1.57, the limits at two standard deviations were 2.89±2.72 and −7.09±2.72 with 95% confidence interval. Finally, comparing AHI_H and AHI_PSG provided the measurement of the accuracy of our method. Correlation coefficient, r=0.97, and under-estimation, slope p=0.76, were found. The distribution of the differences (AHI_H-AHI_PSG) showed a mean of −4.72±3.86 and limits at two standard deviations of 13.29±6.69 and −22.73±6.69 (95% of confidence).

Conclusions: The aim of our study was to show that the measurement of the mandibular movements and a dedicated automatic analysis have a very good potential for the diagnosis of OSAHS. The AHI computed by our automatic method is accurate, reliable and in correlation with the AHI of the gold standard. The recording system of the jaw motion can be used as well in an ambulatory way, as in hospital settings.

O 034
Content comparison of Obstructive-Sleep-Apnea-targeted health status measures in relation to the International Classification of Functioning, Disability and Health

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Aim: The impact of the Obstructive Sleep Apnea/Hypopnea Syndrome (OSAS) on quality of life is not limited to excessive daytime sleepiness. The recognition of the importance of assessing symptoms and functional limitations systematically to optimize the management of the patients with OSAS has led to the development and the use of a number of specific health status measures. OSAS-specific health-status measures and the International Classification of Functioning Disability and Health (ICF)1 represent two different perspectives from which to look at quality of life of OSAS patients.

The objective of our study was to compare the content covered by three OSAS condition-specific health-status measures (the Calgary Sleep Apnea Quality of Life Index (SAQLI), the Functional Outcomes of Sleep Questionnaires (FOSQ), the Obstructive Sleep Apnea Patient-Oriented Severity Index (OASPOSI)) using the ICF.

Methods: OSAS-specific health-status measures were identified and then linked to the ICF separately by two trained health professionals according to ten linking rules developed specifically for this purpose2. The degree of agreement between health professionals was calculated by
means of the kappa statistic. Bootstrapped confidence intervals were calculated.

Results: In the 146 items of the three measures a total of 201 concepts were identified and linked to the ICF. The estimated kappa coefficients is above 0.6 at all different ICF’s levels.

The concepts contained in the items of the measures were linked to 77 different ICF categories, 34 categories of the component body functions, one category of the component body structure, 38 categories of the component activities and participation, and four categories of the component environmental factors. In the component body functions, the categories energy level, sustaining attention, memory functions and emotional functions are covered by all examined measures. 24 categories are covered just by one measure, e.g. heart functions by the SAQ LI. Only the SAQ LI address body structures by evaluating the structure of mouth, namely teeth. In the component activities and participation, only the categories driving, driving motorized vehicles and sexual relationships are covered by all measures. Two measures address environmental factors.

Conclusion: The ICF proved highly useful for the content comparison of OSAS-specific health-status measures. The comparison of selected measures may provide clinicians and researchers with new insights when selecting health-status measures for clinical studies in Obstructive Sleep Apnea.

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O 035
Detection of sleep respiratory disturbance with photo-plethysmography
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Aims: Because of the reportedly high prevalence of Sleep apnea/hypopnea syndrome (SAHS), it is anticipated that demand for screening for this syndrome will soon increase, so that various screening systems are being developed.

Some unresolved problems related to these systems prompted us to focus on the fact that arousal invokes autonomic nervous activity. In this study we examined the dynamics of finger photo-plethysmography to determine whether it is useful for detecting respiratory disturbance (RD) including respiratory effort related arousal.

Method: Polysomnography was used together with photo-plethysmography on baseline night and continuous positive airway pressure (CPAP) titration night for 15 patients with SAHS. After that we examined relationship between RD and plethysmographical dynamics on software.

Result: We identified obstructive and central patterns of RD-specific complexes and those of fused variant. This variant was observed in patients with hypertension. Sensitivity and positive predictive value (PPV) were good for severe SAHS. In mild SAHS and upper airway respiratory syndrome (UARS) subjects declined sensitivity little, but they reduced PPV according to less severity.

RD index (RDI) which is counted with respiratory data had best correlation with the number of these complexes divided by total sleep time (estimated-RDI) than oxygen desaturation index (ODI) 3% or ODI 4%. Correlation coefficients of ODI 3% and ODI 4% and of estimated-RDI were .99, .98, and .99, respectively. Estimated-RDI kept good value even in low apnea/hypopnea index. (r=.71, .68, .94, respectively). This can be a good indicator for estimating RDI especially for UARS or for CPAP titration.

O 036
Assessment of Obstructive Sleep Apnea in Morbidly Obese Patients Referred to Bariatric Surgery
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Aims: To determine the prevalence and severity of Obstructive Sleep Apnea (OSA) as well as the characteristics related to gender for this disease in morbidly obese patients referred to bariatric surgery.

Methods: 78 patients (25 male and 53 female) were consecutively evaluated at Endocrinology Clinic and routinely referred for OSA work up including: 1- Respiratory sleep disorder questionnaire (Fletcher & Luckett) and Epworth sleepiness scale. 2-Measurements of BMI, neck and abdominal circumferences. 3-Full night polysomnogram: performed in Alice 3 System. Apnea and hypopnea Index (AHI) were expressed according to Task Force of Sleep Medicine American Academy including only events with dropped saturation > 3%.

Results: OSA prevalence was 67% in male and 48% in female. Male versus female characteristics (x/sd): Age: 38, 7 ± 14.2 vs 43.6 ± 11.7 years; BMI: 49.1 ± 8.1 vs 48.4 ± 7.6 kg/m²; Neck circumference: 48.4 ± 4.3 vs 40.4 ± 3.2 cm; Epworth scale: 11.5 ± 5.8 vs 9.6 ± 5.8; AHI: 53.7 ± 50 vs 15.8 ± 21.1 (p < 0.01).

Correlations: Male: BMI vs AHI (r = 0.40; ns); Neck circumference vs AHI (r = 0.38; ns); Neck circumference vs
neck circumference vs AHI (r = -0.83, p < 0.01); Epworth scale vs AHI (r = 0.43, ns). Female: BMI vs AHI (r = 0.50, p < 0.01); Neck circumference vs AHI (r = 0.26, ns); Neck circumference vs nadir Sat O2 (r = -0.47, p < 0.01); Epworth scale vs AHI (r = 0.3, ns).

Conclusions: In this population: 1- OSA was more prevalent and more severe in man compared to women. 2- Neck circumference was strongly associated with OSA in man but not BMI, however in women BMI was moderately associated to OSA but not neck circumference.

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O 037
Sleep-Disordered Breathing Surgery: Personal Experience and Procedures Selection Criteria
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Methods: Retrospective evaluation of 854 patients operated between 1998 and 2005, mostly referred by Sleep Lab of Neurologic Clinic, University of Bologna. All the cases were discussed by the Neurological and ENT team before the final treatment planning.

Results: SIMPLE SNORERS: first line operation is UPPP in general anaesthesia, with a mean snoring reduction of about 90%. "Somnas" RFVR may be proposed in an outpatient setting, with a mean snoring reduction of 76%. UARS & OSAHS, RDI & BMI < 30: first line of operation is a nose, palate and hyoid suspension procedure, if a multilevel problem is to be fix. Success rate was of 87.1%. OSAHS RDI > 30, BMI < 30, TS > 3/4: a complete nose, palate and hyoid suspension procedure may be accomplished with a success rate of 64.5%. OSAHS RDI > 30 & BMI > 30, whatever tonsils size: it is treated as first line surgery with Maxillo Mandibular Advancement according Riley & Coll. (1988), with a success rate of 95%, and a good compliance for the patients.

Conclusion: Our criteria proved to be useful for effective surgical procedure selection according to the patient's clinical profile.

O 038
"NOH": A New Scoring System for Classification of upper Airways Collapse Sites in OSAHS
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Aims: A new surgical oriented scoring system for airways collapse in OSAHS is described. As well as in oncological TNM classification, NOH summarizes in a concise formula all the potential obstructive sites, the respective degree and the collapse pattern.

Methods: 3 sites are described: N (Nose & Nasopharynx), O (Oropharynx) and H (Hypopharynx). Informations are obtained by history, fiberoptic endoscopy and lateral cephalogram. Grading of obstruction is classed into five scores: 0 (0% or absent); 1 (1–25% or slight); 2 (26–50% or moderate); 3 (51–75% or severe); 4 (76–100% or complete). The obstruction of O&H is based on Müller manoeuvre (MM). Pattern of collapse in O&H areas is evaluated by MM and noted as anteroposterior (a), lateral (l), circular (c). 84 pts were evaluated for the study.

Results: An high level of statistic significance was demonstrated in interindividual observations, intraindividual correspondence in repeated test, between NOH & OSAHS severity.

Conclusion: NOH classification proved to be an easy and tested tool to define the upper airways collapse sites. Advantages: all sites included, grading of obstruction considered, a low tech required, surgical oriented. Limits: partially subjective, semi quantitative score, shares the limits of the Muller manoeuvre and cephalogram.

O 039
Coblation employed for lingual tonsillectomy in patients with obstructive sleep apnea syndrome: preliminary report
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Introduction: Patients diagnosed with obstructive sleep apnea syndrome (OSAS) who evidence upper airway obstruction secondary to hypertrophic lingual tonsils are difficult to manage. Treatment with the use of sharp as well as electro and laser assisted lingual tonsillectomies is fraught with difficult exposure of the tongue base, bleeding, and severe post-operative pain. Coblation is a new technique, which incorporates a bipolar radiofrequency probe and opens new perspectives in this field.

Aims: To evaluate the safety and post-operative morbidity of lingual tonsillectomy with coblation.

Material and Methods: Nine consecutive patients during period of 2001 -2004 with polysomnographically diagnosed
mild to severe OSAS (median respiratory disturbance index = 13) and lingual tonsils hypertrophy proven by fibrosalangyoscopcy and/or MRI were selected to the study. There were 6 males and 3 females with age range from 18 to 57 years (mean 42.6 ± 14.2 yrs). Lingual tonsillectomies were performed under general anesthesia and direct pharyngoscopy with a coblator II generator (Arthrocare, Sunnyvale, CA). Intraoperative blood loss was measured by graded suction plate; post-operative bleeding was evaluated by clinical signs and fibrosalangyoscopcy on the next post-operative day. Acute post-operative pain was measured using 10-cm visual analogue scale (0-no pain, 10-severe pain).

Results: Our data showed the estimated blood loss to be small ranging from 0.5 ml to 50 ml (mean 23.3 ± 18.7 ml). Procedure time was comparable with the time using other techniques. There was no post-operative bleeding. Acute pain score after operation was mild and ranged from 0 to 7 (mean 3.2 ± 2.7). There was no significant correlation of pain score and severity of sleep apnea.

Conclusions: Data with regard to estimated blood loss, post-operative bleeding and acute pain following lingual tonsillectomy with the use of coblation are encouraging for patients with mild to severe sleep apnea.

O 040
The maturation of sighs and startles during relief from airway occlusion

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We have shown that relief from sleep related airway obstruction is closely related to a cardiorespiratory arousal mechanism including activation of diaphragmatic, submental, mohal muscle groups and heart rate increase as well (Wulbrand 1995). This arousal mechanism is characterized by a sequence of events started by an initial sigh with a startle (Lijowska 1997). It does not to occur as an “all or nothing” event but graded (Wulbrand 1998). Since the intensity of such a mechanism might be crucial for survival of a life resuscitating event during airway obstruction we studied the maturation of sighs and startles during external airway occlusion in 12 normal, healthy infants aged from 34 to 134 days during a daytime nap in terms of magnitudes and timing.

Results: Arousal related defence behaviour during airway occlusion is characterized by a sequence of events beginning with an initial biphasic sigh after 4.8 ± 1.7 SD sec (NON REM)/5.5 ± 2.3 SD (REM) sec. During the second phase of this biphasic sigh a startle occurred accompanied by a neck extension after 6.1 sec ± 2.0 SD/6.5 sec ± 2.6 SD). It was usually paralleled by a head turn, then followed by general body movements (after NON REM: 7.4 sec ± 2.3 SD, REM: 6.7 sec ± 2.3 SD). With growing age the latency of the startle, neck extension and body movement occurrence decreased (NON REM/REM: p < 0.005) while the latency of startle occurrence during a sigh also decreased (NON REM p < 0.01). The intensity of a startle increased (NON REM: p < 0.02) with growing age. Thus during maturation the latencies of the arousal related events are decreasing while the intensity of startles are increasing with age. Impairment of the maturational development of the arousal process might increase the risk of SIDS in terms of upper airway compromise during sleep.

O 041
Pre-eclamptic toxemia is associated with sleep disordered breathing and endothelial dysfunction

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Background: Pre-eclamptic-toxemia (PET) is a common complication of pregnancy, estimated to affect 7%-10% of all pregnancies in the US. The etiology and pathophysiology of the disease are unclear. The disease may be associated with both endothelial dysfunction (ED) and sleep disordered breathing (SDB). We hypothesized that women with PET would demonstrate both SDB and ED, and that a correlation between these two would suggest a potential causative association.

Methods: Seventeen women with PET and 25 matched women with uncomplicated pregnancy have been studied. They underwent a nocturnal ambulatory sleep study (WP100) and non-invasive evaluation of endothelial function utilizing the reactive hyperemia test (Endo-PAT 2000). A higher ratio of post-to pre-occlusion pulse wave amplitude (endothelial function index, EFI) indicates better endothelial function.

Results: Women with PET had significantly higher respiratory disturbance index (RDI) and lower EFI than controls (18.4 ± 8.4 vs 8.3 ± 1.3/h, 1.5 ± 0.1 vs 1.8 ± 0.1, respectively, p < 0.05 for both). Blood pressure significantly correlated with RDI (r = 0.41) and with EFI (r = −0.41, p < 0.05 for both). EFI correlated with birth-weigh of the infants (r = 0.37, p < 0.05), and with RDI (r = −0.28, p < 0.1).

Conclusions: These results suggest that both sleep disordered breathing and endothelial dysfunction are more likely to occur in women with PET than in women with uncomplicated pregnancies. The association between SDB, ED and blood pressure may suggests that respiratory disturbances contribute to or perpetuate the functional abnormality of the blood vessels seen in women with PET.
O 042
Effect of oral appliance therapy for sleep apnea syndrome on blood pressure

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Aims: To evaluate the effect of an oral appliance for the treatment of obstructive sleep apnea syndrome (OSAS) on blood pressure and its factors influencing the efficacy, patients with OSAS were studied before and after insertion of the device.

Methods: One hundred sixty-one patients (121 men and 40 women, mean age 54.3 years) with mild to moderate OSAS (mean apnea-hypopnea index: 17.9) were studied before and after insertion of the mandibular advancement device with the mean interval of 60 days. Systolic, diastolic and mean blood pressure was taken using an automatic blood pressure monitor (132.0 mmHg, 82.1 mmHg, 107.1 mmHg, respectively at baseline). The patients were subdivided into three groups; responder, partial responder and nonresponder group, according to the difference of mean arterial pressure fall after the treatment.

Results: The systolic, diastolic and mean blood pressure decreased significantly (p<0.001) (127.5 mmHg, 79.2 mmHg, 103.4 mmHg, respectively) after the insertion of the device. The oral appliance therapy produced falls in blood pressure (4.5 mmHg, 2.9 mmHg, 3.7 mmHg, respectively). The response was significantly (p<0.001) correlated to the baseline blood pressure. The responders (n=70, mean blood pressure fall > 3.7 mmHg) and the partial responders (n=46, 0 < fall < 3.7 mmHg) showed significantly (p<0.05, ANOVA) higher AHI reduction (69.6%, 65.9%, respectively) than that (52.5%) of no responders (n=45, fall < 0 mmHg).

Conclusions: These data suggest that effective oral appliance therapy for OSAS patients with hypertension can lead to a substantial reduction in daytime blood pressure.

O 043
Association of polymorphisms in the beta2 and beta3 adrenergic receptor genes with obstructive sleep apnea/hypopnea syndrome

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Aim: To investigate the association of polymorphisms in the beta2 and beta3 adrenergic receptor (beta2 and beta3-ADR) genes with obstructive sleep apnea/hypopnea syndrome(OSAHS).

Methods: The genotypes and alleles of beta2 and beta3-ADR genes were identified by polymerase chain reaction-restricted fragment length polymorphism assay in 318 unrelated subjects of North region “Han” population of China(including 165 male OSAHS subjects and 153 male non-OSAHS subjects).The genotypes and allele frequencies of the polymorphisms were compared between OSAHS group and non-OSAHS group. The effects of the polymorphisms in OSAHS group on body mass index(BMI), neck circumference(NC), waist/hip rate(WHR), apnea-hypopnea index(AHI), systolic blood pressure(SBP), diastolic blood pressure(DBP) were analysed.

Results: There were significant differences in genotypes distribution in beta3 -ADR polymorphism between the two groups($\chi^2 = 10.434$, P=0.006). Compared with the control group,OSAHS group had significantly higher Arg allele frequency in beta3 -ADR polymorphism($\chi^2 = 12.742$, P=0.004).There were independent effects of beta3-ADR polymorphism on BMI, NC, WHR in OSAHS group, carriers of the Arg allele of beta3 -ADR polymorphism had greater BMI, NC, WHR, (P=0.019, 0.025, 0.012), while the carriers of the Arg allele had greater AHI and SBP (P=0.032, 0.035), but after adjusted for BMI, AHI and age, there were no differences in SBP between the carriers and non-carriers of Arg allele(P=0.097).There were no significant differences in the genotypes and allele frequencies in bet2 -ADR polymorphism between the two groups($\chi^2 = 1.406$ and 0.809, P=0.465 and 0.382).

Conclusion: beta3-ADR polymorphism may be involved in the development of central obesity and may be related to OSAHS by the central obesity in men OSAHS subjects of North region “Han” population of China,and may be induce hypertension in OSAHS patients of the population indirectly through obesity and sleep apnea, on the contrary, beta2 -ADR polymorphism may not be correlated with central obesity and OSAHS in the population.

O 044
Association of polymorphisms the angiotensin system genes with obstructive sleep apnea/hypopnea syndrome

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Aim: To investigate the association of polymorphisms in the angiotensin system gene with obstructive sleep apnea/hypopnea syndrome(OSAHS).

Methods: The genotypes and alleles of ACE and AGT genes were identified by polymerase chain reaction-restricted fragment length polymorphism assay in 221 unrelated subjects of North region “Han” population of China(including 121 OSAHS subjects and 100 non-OSAHS subjects). The genotypes and allele frequencies of the polymorphisms were compared between OSAHS group and non-OSAHS group. The effects of the polymorphisms in OSAHS group on body mass index(BMI), neck circumference(NC), waist/hip rate(WHR), apnea-hypopnea
index(AHI), systolic blood pressure(SBP), diastolic blood pressure(DBP) were analysed.

**Results**: There were significant differences in genotypes distribution in AGT polymorphism between the two groups (P = 0.009). Compared with the control group, OSAHS group had significantly higher T allele frequency in AGT polymorphism (P = 0.020). There were independent effects of AGT polymorphism on BMI, NC, WHR in OSAHS group, carriers of the T allele of AGT polymorphism had greater BMI, NC, WHR, while the carriers of the T allele had greater AHI, SBP, DBP.

**Conclusion**: AGT polymorphism may be involved in the development of central obesity and may be related to OSAHS and hypertension in OSAHS patients by the central obesity in men OSAHS subjects of North region “Han” population of China, on the contrary, ACE polymorphism may not be correlated with central obesity and OSAHS in the population.
Restless Legs Syndrome

O 045
Changes in dopamine receptor sensitivity during restless legs syndrome augmentation

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RLS augmentation is a common complication of long-term treatment with dopaminergic drugs and reflects an overall worsening of RLS symptoms during treatment (1). Its pathophysiology is unknown. The objective of this study was to investigate a possible relation between RLS augmentation and changes in dopamine receptor sensitivity during chronic long-term treatment with L-DOPA by means of a neuroendocrine challenge.

Methods: Twenty-two treatment-naive RLS patients were included in the sample, with a mean age (SD) of 58.5 years (2.6). The mean (SD) IRLS-score improved during treatment from 24, 8(2.7) to 14,3 (3.2) points (p < 0.05). Fourteen out of the 22 patients were classified as AUG.

In both RLS and control groups, baseline PRL plasma levels decreased following acute administration of L-DOPA. However, the AUC reduction was more pronounced in RLS than in controls (p < 0.05).

Following long term dopaminergic treatment, there was a blunted PRL response to l-DOPA in AUG, when compared to before treatment (p < 0.05).

For the N-AUG group, there were no differences between PRL response at baseline and following long-term treatment.

Conclusion: The results show a blunted PRL response to L-DOPA in AUG, and suggest a mild decrease in dopamine receptor sensitivity during RLS augmentation. We propose that RLS Augmentation is mediated by a downregulation of dopamine receptors that would take place in the course of long-term dopaminergic treatment, resulting in a loss of therapeutic efficacy and an increase in severity of symptoms.

Reference

O 046
Validation of the Augmentation Severity Rating Scale (ASRS): First results from a study of the European Restless Legs Syndrome Group (EU-RLSG)

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Introduction: Augmentation reflects an overall increase in Restless Legs Syndrome (RLS) severity as a result of long-term dopaminergic treatment. The EU-RLSG has created recently the Augmentation Severity Rating Scale (ASRS), specifically designed to measure the severity of augmentation. The 4 items of the ASRS measure the change in severity of specific symptoms during treatment when compared to baseline: (1) earlier onset of symptoms during the day, (2) increase in overall symptom severity, (3) shorter latency to symptoms when at rest, (4) spreading from legs to upper limbs. The difference between the items at the two evaluations is summed up into a 0 to 4 scale (0: no augmentation; 4: maximal severity).

Methods: De novo RLS patients were included in 8 centers in Europe and treated for 6 months with L-Dopa in dosages of up to 500 mg/day, as clinically required to provide adequate relief from symptoms.

Test-retest reliability of the ASRS was assessed by comparing two consecutive assessments at baseline. A subsample of patients underwent consecutive ASRS rating by two independent raters to evaluate inter-rater-reliability. The external validation of the ASRS was performed against an independent expert rating on definite, probable or no augmentation for each patient. Discriminant validity was analyzed by comparing patients with an independent CGI for augmentation rating (no or mild vs. moderate to severe) of independent raters. Following a Delphi consensus among 14 leading international RLS experts, the scores of the 4 items on the ASRS scale were weighted into an ASRS total score (items 1 to 4: 60%, 10%, 10%, and 20%).

Results: 52 out of 63 treated patients (65% females, mean age: 50 years, baseline IRLS score 25.0 ± 5.1) were analyzed for this interim analysis. Patients were treated with a median daily dose of 300 mg L-Dopa (range: 50 to 500 mg). 24 patients experienced definite- and 13 probable augmentation.

Reliability:
- Test-retest: Spearman r = .72
- Inter-rater: r = 0.86 for the ASRS total score. However, reliability was highest for item 1 (r = 0.97), and lowest for item 3b (latency to symptoms at rest, in the morning) (r = 0.79).

Validation of the Augmentation Severity Rating Scale (ASRS)
• The correlations of the 4 items with the ASRS at its maximum severity: 1: $r = .89$; 2: $r = .26$; 3: $r = .65$; 4: $r = .64$.
  - Validity:
• Criterion: The correlation between the maximum ASRS score and an independent expert rating was $r = .71$.
• Discriminant: ASRS total score differed between patients with no/mild augmentation and those with moderate/severe augmentation (median: 0.70 vs. 2.40) ($p = .0085$, U-test).

Conclusions: Preliminary results show that the ASRS is a reliable and valid scale to measure the severity of augmentation during long-term treatment. Due to the need to quantify augmentation systematically for the evaluation of both long-term efficacy and tolerability, the ASRS may become a useful tool to monitor augmentation in clinical trials.

O 047
Growth hormone response to low-dose apomorphine is not altered in patients with restless legs syndrome
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Introduction: In patients with Parkinson’s disease (PD), low-dose apomorphine challenge has been shown to cause a rise in growth hormone (GH) which is independent from levodopa treatment. The rise of GH was interpreted as an increased sensitivity of hypothalamic dopamine receptors because of nigrostriatal dopaminergic deficit [1,2]. The etiology of the restless legs syndrome (RLS) is still unknown. Involvement of the dopaminergic system is assumed to play a pivotal role in the pathophysiology of RLS. The aim of this study was to examine whether the GH response to subcutaneously applied low-dose apomorphine is altered in patients with RLS as compared to healthy controls.

Patients and Methods: We investigated 40 patients with idiopathic RLS (20 patients with levodopa, 20 patients without dopaminergic/RLS-specific treatment) and 20 age- and sex-matched healthy controls by means of the low-dose apomorphine test [1]. GH was analyzed at baseline, as well as 45 and 60 minutes after subcutaneous low-dose apomorphine injection.

Results: 40 RLS patients (58.3 ± 12.0 years, 32 females) with a mean RLS Severity Scale score of 23.9 ± 6.6 (range 10 to 37) and a mean duration of the disease of 99.6 ± 143.1 months were examined. GH was not significantly increased from baseline to 45 minutes after injection (2.4 ± 2.4 ng/ml at baseline vs. 2.7 ± 2.3 ng/ml) nor to 60 minutes after baseline (2.2 ± 1.8 ng/ml). The results were independent from treatment with vs. without levodopa and not different from healthy controls (2.3 ± 3.2 ng/ml at baseline vs. 2.4 ± 2.7 ng/ml 45 minutes after baseline).

Conclusion: As RLS patients did not show a significant increase in GH after stimulation with low-dose apomorphine, the sensitivity of extrastriatal hypothalamic dopamine receptors seems not to be altered in this patient group as it is in PD.

References

O 048
Restless legs syndrome: plasma homocysteine levels in relation to levodopa treatment
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Background: Hyperhomocysteinemia is a risk factor for vascular diseases and potentially for dementia and depression. The most common causes of elevated homocysteine levels are deficiency of folate or vitamin B12 or renal failure. Elevated homocysteine levels have been shown in patients with Parkinson’s disease (PD), particularly in those treated with levodopa.

Objectives: To determine whether changes in plasma homocysteine levels can also be observed in patients with restless legs syndrome (RLS) in relation with levodopa treatment and to determine which role folate and vitamin B12 play in RLS.

Patients and Methods: To date, we investigated 127 subjects, 53 with RLS (23 under levodopa therapy), 47 with PD (28 under levodopa therapy), and 27 healthy controls. Blood samples were collected after overnight fast for the measurement of homocysteine, folate, vitamin B6, and vitamin B12.

Results: Mean plasma homocysteine levels were highest in PD patients (14.2 ± 5.6 μmol/l) and significantly higher than in RLS patients (11.5 ± 3.0 μmol/l; P = 0.009). There was no significant difference of homocysteine levels between RLS patients and healthy controls and in between the two RLS groups (with or without levodopa). RLS patients had a similar disease duration as PD patients (P = 0.109) but levodopa dosages were significantly lower (RLS 239 ± 154 mg vs. PD 440 ± 276 mg; P = 0.001). Homocysteine showed an inverse correlation either with folate or with vitamin B12 in each group.

Conclusions: RLS and in particular levodopa treatment in RLS is not associated with
hyperhomocysteinemia as previously reported and confirmed in this study for PD patients. This might be dose-related or due to other mechanisms. For PD it is discussed that methylation of levodopa and dopamine by catechol O-methyltransferase, an enzyme that uses S-adenosylmethionine as a methyl donor and yields S-adenosylhomocysteine, rapidly converts to homocysteine and thus resulting in increased homocysteine levels. Deficiency of folate or vitamine B$_{12}$ plays a role in elevated homocysteine levels in patients with RLS as well as in PD patients and in healthy controls. Homocysteine levels seem not to be relevant in RLS patients both with or without levodopa treatment.

O 049
A Segregation analysis of Restless Legs Syndrome (RLS)


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Objective: To ascertain the likely inheritance pattern of RLS using a segregation analysis of families of RLS patients ascertained during a case-control study. Background: Familial aggregation has long been suspected in the Restless Legs syndrome, but has received little formal investigation. A segregation analysis done in German families ascertained through an RLS proband found a good fit to a model of dominant inheritance, but only in families having an age of onset below 30(1). 3 candidate regions have been found on different chromosomes in distinct populations using different techniques and models.

Methods: Probands were selected from consecutive RLS patients presenting to the Neurology and Sleep clinics of the Johns-Hopkins Bayview medical center. Patients willing to have first and second degree relatives contacted were included. An RLS diagnosis was made in those who endorsed the four diagnostic features of RLS and whose symptoms could not be explained by an alternate diagnosis. Those with uncertain diagnosis were excluded from analysis. 77 pedigrees were analyzed including 590 phenotyped subjects, 281 of whom had a confirmed diagnoses of RLS. The segregation analysis was carried out using SAGE, analyzing RLS as a dichotomous trait as well as considering age of onset models of RLS.

Results: Considering the analysis of RLS as a dichotomous trait, only the 2-susceptibility models with Mendelian transmission and gender as a covariate had a good fit to these families (P-value=0.05). Non-genetic models and 3-susceptibility models were clearly rejected. The best model indicated a dominant gene with allele frequency of 0.077 and complete penetrance. RLS frequency in subjects lacking the predisposing allele was 0.14. A commingling analysis revealed two underlying distributions of age of onset, with a dichotomy at 26.3 years. Contrary to the dominant model for RLS as a dichotomous trait, age of onset models indicated polygenic inheritance.

Discussion: A dominant model for RLS is consistent with the previous segregation analysis (1). Different linkage analysis results in other populations studied (2) may suggest genetic diversity for RLS causation. The presence of a relatively high frequency, 14%, in those without a susceptibility genotype in our ascertained families further underlines this.

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O 050
Characteristics of RLS in a Severely Affected Support Group Population

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Background and Introduction: The characteristics of RLS patients may vary with their severity. We have examined the clinical characteristics of a series of 60 severe patients with definite RLS who have volunteered for the RLS Foundation brain bank program.

Methods: Patients completed written questions and the International RLS Study group rating scale (IRLS) on entry. They were subsequently interviewed using the Hopkins Diagnostic Interview for RLS, which verified diagnostic features and collected clinical data.

Results: 81% of the patients were female; average age was 71.2 years (SD 12.9). Mean age of onset was 29.9 years (SD 21.8); mean duration of symptoms at current level of severity was 17.4 years (SD 13.7). 21.7% of patients had onset up to age 10, 61.7% had onset up to age 30. The distribution of ages was bimodal with onset in the 5th decade less frequent than onset in either the 4th or the 6th. 90% have daily symptoms without medication. Average IRLS score was 27.8 (SD 6.0) out of 40, in the severe range. Mean Johns Hopkins RLS severity scale was 2.15 (80% had symptoms before bedtime; 35% had symptoms before 18:00 in the afternoon). 36% described their symptoms as painful.
69% indicated that, without medication, their symptoms would last for an hour up to all night. Without medication, 97% would have difficulty sleeping due to RLS; 73% report this would be 5 or more nights per week. 91% are currently receiving treatment. Of these, 66% were using dopaminergic medications (49% agonists; 17% levodopa); 29% were receiving narcotic analgesics; and 20% were receiving medications from more than one class of recommended RLS medications. 75% of patients believed that at least one first degree relative also had RLS. 73 of 310 first degree relatives (23%) were reported to have RLS.

**Summary and Conclusion:** In this bunch of severe RLS patients, symptoms are daily, prolonged, and severely impact sleep. They are a knowledgeable group: most are receiving appropriate treatment for RLS from recognized drug classes. Their symptoms have lasted an average of 40 years and have been highly frequent for almost two decades. Age of onset shows a bimodal distribution, with most patients having an early age of onset. In a large majority of these patients, RLS is familial.

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O 051
Clinical Characteristics of Augmentation during L-Dopa Treatment in Restless Legs Syndrome: Preliminary Results of a European Multicentric Study

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**Introduction:** Augmentation (AUG) is a complication of dopaminergic treatment of Restless Legs Syndrome (RLS). Main features of AUG include an earlier onset of symptoms during the day when at rest, extension to previously unaffected body parts, and a general worsening of symptoms during treatment with dopaminergic drugs (Allen RP et al. 2003).

**Methods:** In 6 European countries, untreated patients with RLS according to current criteria were included, and standard treatment with L-Dopa was initiated. Dosage could be adjusted according to clinical needs up to a maximum dose of 600 mg levodopa. Before start of treatment, and monthly thereafter during a 6-month period, augmentation was assessed along with other severity measures for RLS (IRLS, RLS-6, CGI, RLS-QLI). The presence or absence of augmentation was assessed retrospectively according to NIH criteria (Allen RP et al. Sleep Medicine, 2003) by independent clinical experts in augmentation. Of 63 treated patients, 52 have so far completed the study and 49 could be analyzed.

**Results:** Of the 49 patients (65% females, age 50 years, baseline IRLS score 25.0 ± 5.1), 26 patients (53.1%) had completed the 6-month treatment period and 23 (46.9%) had dropped out. Patients were treated on average with a daily dose of 300 mg L-Dopa (median; range: 50 to 500 mg). Definite augmentation according to NIH criteria occurred in 24 patients (49%) and augmentation was diagnosed by at least one of the 2 experts in further 13 patients (26.5%, at least probable augmentation in 75.5% of the patients). Augmentation occurred in similar frequency in dropouts and in completers. This finding includes that definite augmentation was tolerated in 12 of 26 completers (46.2%). Augmentation occurred on every dose level in comparable frequency: maximum L-dopa dose during the trial ≤100 mg: 1 of 2 patients = 50%, 200 mg: 7/10 = 70%, 300 mg: 14/16 = 87.5%, 400 mg: 11/16 = 68.8%, 500 mg: 4/5 = 80%. L-dopa dosages of at least 300 mg/day had been administered to 78.4% of all patients with probable or definite augmentation. No difference in average dose of L-dopa could be found between patients with probable (312 ± 129 mg) or definite (333 ± 87 mg) augmentation compared to those without augmentation (317 ± 119 mg).

**Conclusion:** Preliminary results suggest that in the course of a six-month treatment period with L-Dopa, AUG occurred definitely in 49% of patients and was probable in further 26.5%. Augmentation was diagnosed on all dose levels of L-Dopa treatment. Even definite augmentation could be tolerated by almost half of the affected patients.

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O 052
Prevalence of Restless Legs Syndrome in Japanese General Population

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**Introduction:** It is well known that prevalence of restless legs syndrome ranges between 5 to 15% in western countries. On the other hand, reports from Singapore and Turkey showed smaller values than those of European and North American populations, suggesting the existence of racial difference in the prevalence of RLS. However, there has been no conclusive information about the epidemiology of RLS in Japanese general population. In order to clarify this issue, we made a cross sectional survey to determine the prevalence, risk factors, and clinical presentation of the disorder in Japanese population.

**Subjects and Method:** This cross-sectional study evaluated 11950 respondents who entered Internet-linked questionnaire survey conducted in August 2004. The items
were designed to ascertain demographic variables, sleep habits and both the existence of RLS by using Japanese version of RLS questionnaires and the severity of the disorder by using IRLSSG rating scale. The severity of sleep disturbance was also measured with Pittsburgh Sleep Quality Index (PSQI). After excluding 1658 samples (13.9%) with invalid answers, the results of 10292 respondents (male = 4833, female = 5459, age ranged from 20 to 79 years) were analyzed.

Results: Probable RLS were found in 429 subjects (4.2%) who fulfilled the every RLS criteria items, and the rate of the disorder was significantly higher in female (4.9%) than in male (3.4%). The rate of the number of probable RLS did not differ by age, and 58.1% of probable RLS subjects answered that their RLS symptom developed before 40 years of age. Multivariate logistic regression analysis revealed that the existence of probable RLS was significantly associated with PSQI score (6 points or more, OR = 1.6, 95% CI: 1.4–2.2). However, 59.7% of probable RLS subjects showed 15 points or less of the value of severity rating scale, and only 12.6% of probable RLS subjects showed 10 points or more of PSQI score. In addition, the rate of probable RLS subjects who sought medical assistance was only 8.2%.

Discussion: Our results indicated that the point prevalence of probable RLS in Japan was higher than the results from Singapore and Turkey, and the existence of the disorder was thought to play a certain role on the occurrence of insomnia. However, severity of RLS and its influence on sleep disturbance were thought to remain mild degree in majority of our probable RLS population. The female predominance we found for RLS was compatible with most of the previous reports. Although RLS has been recognized to be a disorder primarily of middle age and old age, we found an early age at onset of the disorder in this study. This finding is compatible with one report from Turkey1), suggesting that RLS is probably more common than heretofore recognized among young people.

Reference

O 053
The prevalence of symptoms of Restless Legs Syndrome in young Finnish adults

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Aims: To determine the prevalence of restless legs syndrome (RLS) in young Finnish adults in a cross-sectional survey.

Methods: A representative sample of 23-year-old Finnish adults was sent a questionnaire. Questions about RLS were asked using items recommended by the International Restless Legs Study Group. In addition, questions about other medical disorders, sociodemographic data, life habits, and life satisfaction were asked.

Results: Altogether 885 persons (379 men and 506 women) responded. The median body mass index was 22.3 kgm-2 (23.2 in men and 21.6 in women; P < 0.001). 34.1% of men and 23.2% of women smoked daily. 5.2% (N = 47) of the responders had Swedish as their native language (Finnish-Swedish families). Using the IRLSSG criteria with all four main symptoms present at the same time the prevalence of RLS was 7.6% (5.6% in men and 9.1% in women; P = 0.056). The prevalence of RLS with disabling symptoms at least once a week was 2.3% and the prevalence of RLS with symptoms at least on 3 days per week was 1.1% (0.5% in men and 1.6% in women). 50.0% of the subjects with RLS and 23.7% of the others suffered from symptoms of anxiety or uneasiness at least once a week (P < 0.001). Difficulties to fall asleep or disturbed sleep at least once weekly were more common (P = 0.001) among subjects with RLS (45.5%) than among the others (26.2%). At least weekly occurring headache was significantly more common (P < 0.001) among those with RLS (42.3%) than among those without RLS (18.5%). Life dissatisfaction was slightly more common in those with RLS (LS-score 9.13) than in those without RLS (LS-score 8.48), as was smoking (36.4% of RLS patients smoked daily vs. 27% in those without RLS). Neither of these differences was statistically significant. RLS was more common (P = 0.039) among the Swedish-speaking participants (10.6%) than among Finnish-speakers (4.7%).

Conclusions: The prevalence of restless legs syndrome is 7.6% among young Finnish adults aged 23 years. RLS is associated with sleep disorders and headache and it may have a negative impact on quality of life at that age. The prevalence of RLS among Swedish-Finnish and Finnish families needs to be studied further before drawing conclusions from a difference in occurrence and from possible reasons for it.

O 054
Unilateral Restless legs syndrome-association with degenerative disc disease

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Aim: Restless legs syndrome (RLS) is generally known to affect lower limbs and in some patients, upper limbs, symmetrically. Unilateral restless legs syndrome has been reported to occur in only a small percentage of patients. The
aim of the present study was to study patients with unilateral RLS presenting to our Sleep disorders Clinic.

Methods: We studied 37 patients of idiopathic RLS seen over a period of one year between January 2004 and January 2005. Detailed sleep disorders questionnaires were filled for all patients. All details of the RLS were recorded, including the diagnostic criteria as well as description, distribution, timing, severity of precipitating and relieving factors of symptoms and details about coexisting illnesses and treatment were recorded. Results of investigations were recorded.

Results: We identified 4 patients (3 females, 1 male) of age ranging between 27 and 55 years, who presented with RLS involving one sided lower limb, either isolated or predominantly, with gross asymmetry. All these patients had significant lumbosacral degenerative disc disease, which was silent in one patient. One of these patients also had symptoms involving the upper limb on the same side. The RLS symptoms were independent of radial pain and paraesthesiae, which had different distribution and timing of occurrence.

Conclusion: Since patients with lumbosacral radiculopathy usually present with unilateral or asymmetrical symptoms, symptoms of RLS can be easily overlooked, especially if the distribution is asymmetrical. Treatment with dopaminergic agents can almost completely relieve the discomfort associated with RLS, without much change in the radicular symptoms, however leading to much improvement in quality of life. Significance of this association is being discussed.

O 055
Rise of Blood Pressure as a component of autonomic arousal with Periodic Limb Movements in Sleep in patients with Restless Legs Syndrome

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Background: Blood pressure monitoring in 1 patient with PLMS was documented more than 10 years ago which showed a rise associated with the PLMS. Various studies have demonstrated a change in pulse rate with PLMS. This study is done to demonstrate any change in blood pressure with PLMS and to correlate these changes in blood pressure with changes in pulse rate at the time of PLMS.

Objective: To determine changes in blood pressure associated with Periodic Limb Movements in Sleep (PLMS) in patients with Restless Legs Syndrome (RLS).

Design/Methods: Three female patients ages 30 yr, 60 yr and 66 yrs with RLS and PLMS were asked to lie in bed prior to polysomnography and imitate PLMS which were recorded with EMG. The patients were asked to flex the right foot alternating with the left foot every 10 seconds for 5 minutes. Any involuntary PLM during wakefulness were recorded as were PLMS during sleep. Blood pressure and pulse rate were continuously monitored under all three of these conditions. Changes in blood pressure and pulse rate at the time of PLM were compared under these three conditions. The data was analyzed blindly and the technical faulty readings were excluded. This is our preliminary data and the study is till in progress.

Results: For the 3 patients 165 involuntary PLMS during sleep and 32 voluntary PLM in wakefulness were analyzed. There was a rise in blood pressure noted after the voluntary imitated PLM of 2.5 mm Hg in systolic blood pressure and 1.5 mm Hg in diastolic blood pressure which persisted for 7–10 sec after the movements. There was a rise in blood pressure noted after the involuntary PLMS in sleep that was higher and more persistent (11.4 in SBP and 5.8 in DBP mmHg for 7–10 sec). An examination of 33 involuntary PLM in wakefulness also suggest a rise that was much higher than noted with the voluntary PLM in wakefulness. We also noted that there was a much higher rise in SBP and DBP after respiratory related limb movements. For all 3 conditions the pulse rate also increased with a magnitude proportional to that seen with the rises in blood pressure.

Conclusions: This is our preliminary data and the movements studied are few in numbers to draw any conclusions. The study is still in progress. There was a rise in blood pressure and pulse rate noted during involuntary PLM in sleep and wakefulness which exceeded that seen with voluntary mimicked PLM in wakefulness. The rise in the blood pressure and pulse rate can be a component of autonomic arousal seen with PLMS. Since most patients with RLS have PLMS, the rise of blood pressure in patients with PLMS may be an indicator of the previously noted association of hypertension and heart disease with RLS.

O 056
Cabergoline compared to levodopa in the treatment of patients with severe Restless Legs Syndrome: Results from a multi-national, multi-center, randomized, double-blind, active controlled trial

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Introduction: We report the first large-scale double-blind, randomized study to compare two active
dopaminergic therapies for Restless Legs Syndrome (RLS), the dopamine agonist cabergoline (CAB) and levodopa/benserazide (LEV). The aim was to demonstrate (a) non-inferiority in symptom relief of CAB compared to LEV after 6 to 8 weeks of short-term treatment and (b) superiority of CAB over LEV after 30 weeks of long-term therapy regarding insufficient treatment outcome.

Methods: Patients with idiopathic RLS were treated with fixed daily doses of 2 mg CAB or 200 mg LEV; in the event of insufficient efficacy after six weeks, dose was increased to 3 mg CAB or 300 mg LEV. Efficacy was assessed by changes in the IRLS (International RLS Severity Scale) to evaluate non-inferiority after short-term treatment. For long-term superiority evaluation, time to discontinuation of treatment due to lack/loss of efficacy or augmentation and rate of affected patients according to investigators’ assessments was analyzed.

Results: 361 of 418 screened patients (age 58 ± 12 years, 71% females) were randomized and treated (CAB: n = 178; LEV: n = 183) in 51 centers of 4 European countries. Baseline IRLS total score was 25.7 ± 6.8 which corresponds to “severe” intensity of RLS in the study population. Dose increase was more frequently required in LEV patients (49.4%) vs. CAB (24.1%, p<.001).

The adjusted mean change from baseline in IRLS sum score in the short-term period was d = −16.4 in the CAB group and d = −10.1 in the LEV group. The 5% confidence interval of the adjusted mean difference between both treatments at the end of the short-term period, [-8.4; -4.3, point estimate: -6.4] demonstrated not only non-inferiority, but also a clinically significant superiority of CAB over LEV (p<.0001). Of all patients, 58.8% in the CAB group and 32.2% in the LEV group (p<.0001) improved by at least 50% of the baseline IRLS score at individual study end.

During the total treatment period of 30 weeks, more patients of the LEV group (24.0%) than of the CAB group (11.9%, p = .0029, log-rank test) discontinued due to lack/loss of efficacy (14.2% vs. 7.9%, p = .0290) or augmentation (9.8% vs. 4.0%, p = .0412). Adverse events (AEs) required premature discontinuation from the trial in 21.3% of the patients treated with CAB and in 14.2% of those with LEV. Drug-related AEs occurred in 67.9% of the CAB group and in 50.2% of the LEV group. Most frequently, gastrointestinal AEs were reported (CAB: 54.1%, LEV: 32.4%).

Conclusions: This first large-scale active controlled study in RLS showed superior efficacy of cabergoline vs. levodopa after short- and long-term therapy. Discontinuation from treatment due to loss of efficacy or augmentation was less frequent under cabergoline than under levodopa. For levodopa, the rate of augmentation or poor efficacy over a 30-week period under double-blind conditions was 24% which is surprisingly low compared to data from open-label or retrospective trials.

O 057

Sustained efficacy of Pramipexole in Restless Legs Syndrome

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The short-term efficacy of pramipexole (PPX) in the treatment of Restless Legs Syndrome (RLS) is established by placebo controlled and open label studies. Moreover several publications suggest that PPX is efficacious in the long-term treatment of RLS patients, but the evidence is based on open label or retrospective studies. The current study was conducted to provide proof of sustained efficacy using a placebo-controlled randomized withdrawal design.

Methods: The International RLS Severity Rating Scale (IRLS) and the Clinical Global Impression-Improvement (CGI-I) were used as clinical rating instruments.

Design: The study had two periods. In period 1 idiopathic RLS patients (18–80 years) with moderate to severe RLS (measured by the IRLS >15) were enrolled and treated with open label PPX (dose range 0.125–0.75 mg/d) for 6 months. Treatment response at month 6 was defined by a IRLS score <15 and a Clinical Global Impression-Improvement (CGI-I) of much or very much improved compared to baseline.

In period 2, responders were randomised to double-blind placebo or maintained at the same dose of PPX as at the end of period 1. The primary endpoint for this second period was time to worsening as defined by a IRLS score worsened to >15 and a CGI-I rating of at least “minimally worse” when comparing the status to start of period 2.

Results: 224 patients (64 male (28.8%), 158 female (71.2%)) were enrolled in period 1. Of these, 147 patients (65%) were randomised as responders to period 2. Time to worsening was statistically significantly later in the PPX group compared to the placebo group, p<0.0001, and the proportion of patients that worsened in the PPX group was statistically significant smaller compared to the placebo group (20.5% vs. 85.5%, p<0.0001).

The most frequently reported adverse events (>5%) in the open label treatment period 1 phase were fatigue 17.4%, headache 12.9%, and nausea 8.9%. In period 2, the db phase, only “worsening of RLS symptoms” was reported in more than 5% of the cases (5.6% placebo, 6.4% in PPX). Most of the AE were of mild or moderate severity. No episode of sudden onset of sleep was reported even when patients at each visit were specifically asked about this AE.

Conclusion: Discontinuation of pramipexole treatment in responding patients with moderate to severe RLS leads to rapid worsening in most patients. This study thus proved in a controlled withdrawal study design the sustained efficacy and safety of PPX in RLS.
Pramipexole is efficacious and safe in treating RLS patients: Results of a 12 weeks placebo controlled, fixed dose study

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Several previous controlled short-term trials up to 6 weeks have shown that pramipexole (PPX) improves RLS symptoms. This new study was performed to evaluate the efficacy and safety of three doses of PPX (0.25 mg, 0.5 mg, and 0.75 mg) compared to placebo in a double-blind, fixed dose, parallel group design. The study had two primary efficacy endpoints: mean change from baseline to end of study in the International RLS rating scale of severity (IRLSRS), and responder status using the Clinical Global Impression-Improvement (CGI-I) scale score at week 12, assessed by different raters.

Weeks 1–4 were used to up-titrate patients to their randomised dose group. According to this design patients were on maintenance treatment from week 5 at the latest until to the end of the study.

345 patients (129 male [38%], 211 female [62.2%]) were randomised to treatment, and 339 patients could be analysed. PPX produced in all dose groups statistically significant greater improvements than placebo in IRLSRS total score at week 12 in all dose groups (adjusted mean change from baseline, Placebo -9.3, PPX 0.25 mg -12.8; \( p = 0.0086 \), PPX 0.5 mg -13.8; \( p = 0.0011 \), PPX 0.75 mg -14; \( p = 0.0005 \)). Similarly, PPX treatment was associated with significantly greater improvement than placebo in CGI-I scores, as measured by the percentage of patients meeting the criterion for a responder (much/very much improved): Placebo 51.2%; PPX 0.25 mg 74.7%; \( p = 0.0005 \), PPX 0.5 mg 67.9%; \( p = 0.0484 \), PPX 0.75 mg 72.9%; \( p = 0.0038 \).

Pramipexole was generally well tolerated. The most frequent AEs by randomised treatment group in more than 5% of PPX patients were nausea (19%), headache 17.8%, RLS 12.8%, insomnia 10.5%, somnolence 10.1%, dizziness 9.7%, nasopharyngitis 6.6%, and fatigue 5%. Two patients reported an episode of sudden onset of sleep with PPX, one patient with placebo. Most AEs were of mild to moderate intensity.

This study confirms the short term efficacy and safety of PPX in the treatment of RLS in a 12 week fixed dose design.
Periodic Limb Movements

**O 059**

**Differential Effects of Aging on Periodic Leg Movements and Associated Cortical Arousals during NREM and REM Sleep in Healthy Subjects**

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**Aim:** In healthy subjects without sleep disturbance the incidence of periodic leg movements (PLMs) and related arousals increases with advancing age. In the present paper, we report the number of PLMs and PLMs associated with cortical arousals in NREM and REM sleep in a large population of healthy controls of all adult age groups, collected within the European multi-center project SIESTA.

**Methods:** Leg movements (LMs), PLMs, as well as arousals according to ASDA rules were automatically identified by means of the Somnolyzer 24x7 in the polysomnographic recordings of 189 healthy volunteers. Subsequently, the number and the index of all events (LMs, PLMs) and events associated with arousals were computed for the time in bed, total sleep time, sleep stages, and REM and NREM sleep. The effects of age on the measures obtained were investigated by applying Spearman rank correlations.

**Results:** In all 3 age groups (29 males, 30 females aged 20–39 years, 27 males, 30 females aged 40–59 years and 34 males and 39 females aged 60 years and above), LMs and PLMs were highest during stage W and decreased with increasing depth of NREM sleep. In young healthy controls, LMs and PLMs dominated in REM sleep (PLM index for NREM: 2.1; for REM: 4.6; p < 0.001). While in middle-aged subjects no significant differences between NREM and REM events were found (PLM index for NREM: 11.5; for REM: 7.7; n.s.), in elderly subjects LMs and PLMs were higher in NREM than in REM (PLM index for NREM: 34.8; for REM: 14.4; p < 0.001). Considering only LMs and PLMs associated with arousals, NREM and REM events did not differ in young subjects (PLM index with arousals for NREM: 0.1; for REM: 0.1; n.s.), but in middle-aged (PLM index with arousals for NREM: 0.7; for REM: 0.2; p < 0.001) and older subjects (PLM index with arousals for NREM: 3.0; for REM: 0.3; p < 0.001).

**Discussion:** The increase in the PLM index with age observed in healthy controls without sleep disturbance, which was more pronounced during NREM than during REM sleep, might be interpreted as an indicator of the normal process of ageing associated with a loss in dopaminergic function.

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**O 060**

**Pathophysiology of periodic leg movements in sleep: A comparative electrophysiological study**

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**Background:** Periodic leg movements in sleep (PLM) are frequently accompanied by EEG-signs of arousal or sleep instability, but the significance of these changes for the pathophysiology of PLM is not well understood. In particular, it is not clear whether PLM are the cause or the consequence of arousals.

**Methods:** Whole-night polysomnographies (PSG) of 24 subjects fulfilling the criteria of either periodic leg movements disorder (N = 8, PLMD), obstructive sleep apnea syndrome (N = 7, SAS), or normal PSG (N = 9) were selected. Spectral EEG- and heart rate-changes were analyzed by calculating the event related synchronization/desynchronization and the heart rate variability, respectively. Changes associated with PLM were compared to changes associated with non-periodic (Non-PLM) and respiratory related leg movements (RRLM). Furthermore, the influence of sleep stage and movement pattern (amplitude, duration, interval, leg moved) on spectral EEG and heart rate changes was assessed.

**Results:** All types of leg movements were preceded and associated with largely the same temporal sequence of heart rate- and EEG-changes, beginning up to 8 seconds before movement onset with an increased heart rate variability and an increased Delta-activity, then showing an increased Theta-, Alpha-, Beta- and Gamma-activity, and ending with a decreased spindle-activity after movement onset. These changes occurred symmetrically over both hemispheres, were sleep stage dependent but independent of movement type, periodicity and moved leg. Neither the EEG- nor the heart rate-changes were correlated with movement amplitude, duration, or interval. However, absolute heart rate variability had greater peaks for PLM than for Non-PLM and RRLM, and Gamma-synchronization began 1–2 seconds earlier for Non-PLM and RRLM than for PLM.

**Conclusion:** All types of leg movements in sleep are clearly preceded by autonomic changes and Delta-bursts, which point to a brainstem activation. This activation seems to progressively ascend to the cortex, as indicated by increased high-frequency EEG-oscillations. No direct and specific marker of the PLM triggering processes in the brain is manifested in surface EEG and ECG. However, EEG signs of cortical arousal clearly preceded Non-PLM and RRLM, but began only shortly before or at the same time as PLM. Also, one marker for brainstem activation peaked more for PLM than for Non-PLM. Therefore, PLM are more
likely to be triggered directly by brainstem processes than by a cortical arousal.

Other Movement Disorders

O 061
Is the amount of nigrostriatal dopaminergic degeneration associated with daytime sleepiness in patients with Parkinson’s disease?

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Introduction: Many patients with Parkinson’s disease (PD) report daytime sleepiness. Dopaminergic drugs are known to play a role in daytime sleepiness in PD patients, its etiology, however, is still not known. The aim of this study was to examine whether the amount of nigrostriatal dopaminergic degeneration is associated with subjective daytime sleepiness and sleep quality in patients with PD.

Patients and Methods: We investigated 21 patients with PD by means of [123I] FP-CIT-SPECT (DaTSCAN). Each patient filled in the Epworth sleepiness scale (ESS), the Parkinson’s Disease Sleep Scale (PDSS), and the self-rating depression scale according to Zung (SDS) to assess sleepiness, sleep, and depressive state. We used Spearman’s rank test to correlate the ESS and PDSS scores with the mean nigrostriatal dopamine transporter binding (DAT).

Results: The mean specific dopamine transporter binding in all 21 PD patients (60.8 ± 10.4 years, 9 females, median Hoehn and Yahr stage 2.0) was 1.45 ± 0.54 in the striatum, 1.16 ± 0.56 in the putamen, and 1.69 ± 0.57 in the caudate nucleus. Nine patients were in Hoehn and Yahr stage 1 (58.7 ± 6.6 years, 4 females; ESS score 7.4 ± 4.5; PDSS score 105.1 ± 30.9), the other 12 patients were in Hoehn and Yahr stage 2 (62.4 ± 12.6 years, 5 females; ESS score 6.7 ± 4.7; PDSS score 97.1 ± 25.6). Age, gender, ESS, and PDSS scores were not significantly different in both groups. However, ESS scores showed an inverse correlation with mean DAT binding in the striatum (r = -0.627, p = 0.03), the caudate nucleus (r = -0.708, p = 0.01), and the putamen (r = -0.599, p = 0.04) in patients with Hoehn and Yahr stage 2. There was no correlation of the ESS score with age, disease duration, UPDRS motor score, PDSS score, or depression score. PDSS score did not correlate with nigrostriatal DAT binding.

Conclusion: Subjective daytime sleepiness but not sleep quality seems to be associated with the dopaminergic nigrostriatal degeneration in PD. Studies with a broader spectrum and more advanced PD patients and with objective measurements of daytime sleepiness are warranted to further confirm this finding.

Parasomnia

O 062
Frequency of Parasomnias in patients with Nocturnal Frontal Lobe Epilepsy (NFLE) and their relatives

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Aims: To verify whether patients with Nocturnal Frontal Lobe Epilepsy (NFLE) and their relatives have a higher frequency of parasomnias, in particular arousal disorders, and to clarify the physiopathological mechanisms underlying NFLE. The aim of the study was to investigate the frequency of parasomnias in patients with NFLE using a questionnaire based on the minimal criteria for diagnosis of parasomnias of the International Classification of Sleep Disorders-Revised (ICSD-R).

Patients and Methods: Patients with NFLE: patients aged >1 year with video-EEG recording of at least 1 hypermotor seizure or 2 paroxysmal arousals; Relatives of patients with NFLE: at least 7 members of the proband family; Control subjects: aged >1 year, matched for age, sex, education and geographic origin. Relatives of control subjects: at least 7 members of the control family. Each subject underwent a standardized interview, applying the ICSD-R minimal criteria to diagnose the main parasomnias occurring at any time in the subject’s life.

Results: 358 individuals were interviewed: 26 patients with NFLE (M/F: 13/13), 161 relatives of probands, 20 control subjects and 151 relatives of controls. The following parasomnias were more frequent in the NFLE group: Probands vs controls: bruxism was more frequent among NFLE probands (p < 0.05). Proband relatives vs control relatives: arousal disorders and nightmares were more frequent among NFLE proband relatives (p = 0.0186) (p = 0.002).

Conclusions: We found a higher frequency of bruxism in patients with NFLE and of arousal disorders in their relatives. These findings suggest some physiopathological mechanisms common to parasomnias and NFLE.

O 063
New findings in muscle tone analysis in patients with idiopathic REM behaviour disorder (RBD) and narcoleptics with RBD

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Aims: We investigated differences in muscle tone during REM-sleep and its distribution in patients with idiopathic RBD (iRBD) and narcoleptics with RBD (nRBD).

Methods: Polysomnographies and videos of 10 iRBD (mean age 38 years) and 22 nRBD patients (mean age 61.1 years) were evaluated for muscle activity during REM sleep. Muscle activity was calculated in percent for each REM-phase separately for the mentalis, left and right tibialis muscle. Muscle activity during 1 epoch was scored if it lasted > 0.5 sec., and if amplitudes exceeded 50% of the preceding atomic EMG baseline in REM-sleep or if at least 10 muscle activities lasting <0.5 sec. occurred.

Results: Mentalis muscle tone in both groups was 2–3 times higher than that of the tibialis muscles. Although medical history of RBD displayed higher frequency and more violent behaviour in iRBD than nRBD, 4 iRBD patients had very low percentage of muscle tone (range 0, 33–6.8%) compared to 5 nRBD (1.5–7.5%). Muscle tone in both groups did not show significant differences for any REM-period. In nRBD mentalis muscle tone decreased throughout the night, whereas it remained at high level in iRBD. From second REM-period on the mean of mentalis activity was always higher in iRBD, whereas activity of the tibialis muscle did not show any changes.

Conclusions: Although muscle tone is elevated in nRBD and iRBD throughout the night, the distribution within both groups seems to be different. Our findings also show different regulation of muscle tone of extremities compared to mentalis muscle. Comparison of automatic analysis of amplitude for each second and visual scoring are presented.

Hypersomnia

O 064
Results of the forced awakening test in 120 consecutive patients complaining of excessive daytime sleepiness

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The comparison of event related potentials (ERPs) obtained during wakefulness and after 3 minutes of sleep (the “forced awakening test”) has been recently proposed to assess simultaneously sleep propensity and sleep inertia in patients with excessive daytime sleepiness (EDS) (Bastuji et al 2003).

We now report our experience in 120 consecutive EDS patients, aged 16–73 years, 50% women, whose etiological diagnosis was narcolepsy (27%), idiopathic hypersomnia (30%), sleep apnea syndrome (SAS) (26%) and EDS associated with psychiatric disorders (17%). On forced awakening, ERPs were abnormal (i.e. presented sleep negativities and/or P300 delay) in 75% of narcoleptics, 74% of patients with idiopathic hypersomnia, and 43% of patients with SAS. On the contrary, forced awakening ERPs were never abnormal in EDS associated with psychiatric disorders. Furthermore, the ERP pattern during forced awakening was significantly related to the aetiology of EDS (X2: 36.7, p=.0001). The presence of sleep negativities on the ERPs following forced awakening was a sign of severe acute sleep inertia, frequently observed in narcolepsy (58%) and idiopathic hypersomnia (59%). The fact that this profile was observed in only 13% of SAS may reflect the difficulty of these patients to quickly deepen their sleep, due to their respiratory disturbances. The behavioural performances in detecting targets were significantly less effective than ERPs to discriminate EDS aetiology. Sleep latencies were abnormal (<7 min) in 87% of narcoleptics, 74% of patients with idiopathic hypersomnia, 78% of patients with SAS and 12.5% of patients with psychiatric disorders. The ERP pattern was not correlated with cataplexy in narcoleptic patients, but rather with the amount of psychostimulant drugs needed during the follow-up (X2: 12.1, p=.02).

Increased sleep propensity, reflected by reduced sleep latency, was frequently associated with ERP abnormalities in FA, but the 2 variables were dissociated in 34% of the cases, indicating that they measure different aspects of EDS. Furthermore, the significant correlation between result on the test and the severity of EDS suggests that the FA test is useful in clinical routine, not only for accurate diagnostic classification, but also as a reliable estimation of the overall severity of EDS.


REM-Sleep-Behaviour Disorder

O 065
Dream content and daytime aggressiveness in REM sleep behavior disorder (RBD)

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Aims: Nocturnal vigorous motor activity associated with dream mentation characterize the REM sleep behavior disorder (RBD). Action-filled and violent dreams are typically reported by patients with RBD, but no study has systematically assessed dream content in this condition. The aims of this study was to evaluate dream characteristics and daytime aggressiveness in patients with REM sleep behavior disorder (RBD).

Methods: Forty-nine patients with polysomnographic-confirmed RBD diagnosis and 71 age and gender-matched controls were initially enrolled in the study. Subject were asked to recall most recent dreams and to fill in the Aggression Questionnaire (AQ) and the Beck Depression Inventory (BDI). Forty-one RBD patients (81.6%; 36M,5W; mean age: 67.5 ± 7.5 yrs.) and 35 controls (49.3%; 30M,5F; mean age: 69.1 ± 5.9 yrs.) were able to remember their dreams and a total of 98 and 69 dreams were collected in the two groups. Verbatim dream description was recorded by a trained interviewer and scored according to the Hall and Van De Castle coding system. Coded dreams were processed by dreamSAT software and differences in dream categories were evaluated with Cohen’s “h” statistic. Between-group differences in both AQ and BDI scores were assessed using t-test and Bonferroni correction was applied for multiple testing.

Results: The mean duration of symptoms in RBD patients was 6.1 ± 6.9 yrs and the mean age at the onset of the parasomnia was 60.8 ± 9.3 yrs. A total of 96 and 63 dreams were collected in RBD and controls, respectively. • RBD patients showed a higher percentage of dream with at least one aggressive episode (DWA) than controls (66% vs.15%; p < 0.00001), a higher aggression/friendliness interaction ratio (86% vs.44%; p < 0.0001) and a greater frequency of animals characters (19% vs.4%; p = 0.0001). In contrast to controls, none of RBD patients had dreams with elements of sexuality (0% vs.9%; p < 0.0001). The two groups did not differ in total AQ scores, except for a lower score on the physical aggressiveness subscale in RBD (16.5 ± 6.4 vs.20.4 ± 8.3; p = 0.034). No correlation was observed between dream aggressiveness and either age, education, duration or frequency of RBD symptoms, or BDI scores (11.0 ± 7.3 vs. 7.8 ± 7.8; p = 0.10).

Conclusions: Dreams in RBD patients appear to be highly stereotyped compared to those reported by healthy subjects. An elevated proportion of aggression themes and animal characters, together with a reduced percentage of sexuality elements, characterizes the dreams in RBD, despite normal levels of daytime aggressiveness. The increased aggressiveness of dream content and the excessive REM sleep phasic EMG activity in RBD may be related to the hyperactivity of a common neuronal generator.

O 066
Classification of motor events in patients with REM sleep behavior disorder

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Aims: REM sleep behavior disorder (RBD) was first described in 1986 by Schenck and Mahowald. According to the International Classification of Sleep Disorders (ICSD), minimal diagnostic criteria of RBD include the presence of limb or body movements associated with dream mentation plus one of the following: harmful or potentially harmful sleep behavior, “acted out” dreams, or sleep behavior disruptive of sleep continuity [1].

The aim of this study was to improve characterization of RBD by classifying motor events using video analysis.

Methods: A total of 9 polysomnographic records from five patients with Parkinson syndrome (Parkinson disease, n = 3; multiple system atrophy, n = 1; Lewy body dementia, n = 1) (mean age, 64 ± 8.7 years) who fulfilled the clinical and polysomnographic criteria of symptomatic RBD was analysed. All patients were on dopaminergic treatment. Subjects were studied at the sleep laboratory of Innsbruck Medical University, Department of Neurology. Sleep stages were classified according to the criteria of Rechtschaffen and Kales. In epochs classified as REM sleep, the video was screened for motor events by a neurological resident trained in sleep medicine. Each event was classified according to type of movement, body parts involved, duration and movement series, if applicable.

Results: A total of 21 REM episodes was recorded (mean duration of REM sleep, 31.1 ± 17.7 minutes per patient and night). Overall, 1392 motor events observed during stage REM were analysed.

63.1% (878) of motor events were classified as single or minor movements (e.g. twitching, little jerks), 12.1% (169) as scenic movements (e.g. searching, laughing, pointing), 10.7% (149) as stereotype (e.g. fidgeting, smacking) and 3.6% (50) as violent movements (e.g. hitting, struggling). 63% (877) of events were isolated, 19% (265) appeared in sequences, 12.9% (180) in an intermittent pattern and 5.2% (72) in a burst pattern. 31.6% (440) of events were classified as segmentary, 26.9% (374) as focal, 24.9% (347) as multifocal and 14.2% (198) as generalized events. Violent behavior was significantly associated with arousals (p < 0.001).

Discussion: These data demonstrate that patients with symptomatic RBD exhibit very high numbers of motor events during REM sleep. However, most events are minor movements, whereas violent episodes represent only a small fraction of motor events.

References

O 067
Rem Sleep Behavior Disorder and Potassium Channel Antibody-Associated Limbic Encephalitis
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Aim: REM sleep behavior disorder (RBD) is caused by dysfunction in the brainstem or elsewhere projecting to this region, such as the limbic system. The aim of our study was to describe the occurrence of RBD in five of six patients registered in our center with non-paraneoplastic limbic encephalitis associated with antibodies to voltage-gated potassium channels (VGKC-LE).

Methods: Clinical interview with the patients and bed partners and video-polysomnography was used to diagnose RBD.

Results: Five men with a median age of 65 (range, 51–72) years presented with subacute onset of memory impairment, confusion, seizures, MRI hyperintensity in both limbic systems sparing the brainstem and other brain areas, negative paraneoplastic antibodies, and high serum titers of VGKC antibodies (median 992 pM, range 300–6254). None of the patients had symptoms or signs that suggested involvement of the brainstorm. Patients’ wives noticed that their husbands displayed dream-speaking behaviors such as shouting and gesturing that occurred since the onset of the memory and behavioral changes. If awakened, patients recalled fearful dreams. In three of them, video-polysomnography showed REM sleep without atonia, increased REM sleep muscular phasic activity associated with excessive limb jerking and no epileptiform activity. In the remaining two, polysomnography was not performed. None of the four patients were treated with clonazepam or any specific therapy for RBD. In three patients, immunosuppressive treatment during one year resulted in complete gradual resolution of RBD symptoms and characteristic video-polysomnographic abnormalities (REM sleep muscular atonia was restored and no abnormal behaviors were detected), in parallel with complete remission of the limbic encephalitis syndrome and MRI abnormalities in the limbic system. RBD persisted in two patients with partial resolution of the limbic encephalitis syndrome.

Conclusions: RBD may be caused by a primary lesion in the limbic system, may have a reversible autoimmune-mediated origin, and is frequent in subjects with VGKC-LE.

O 068
REM behaviour disorder and epileptic phenomena: aspects of the comorbility
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Episodes of REM Behavior Disorder (RBD) can be misdiagnosed, on the clinical grounds, as nocturnal epileptic seizures, namely temporal or frontal lobe seizures (1). The coexistence of RBD/epileptic seizures or the occurrence of EEG interictal epileptiform abnormalities (IEA) in a subject with RBD may increase the likelihood of misdiagnosis. Furthermore, the comorbidity of epileptic phenomena and RBD may be of interest from a physiopathological point of view. In experimental kindling of epilepsy, REM without atonia or REM with EEG synchronization facilitates the occurrence of epileptic phenomena (2).

Coexistence of RBD and epileptic seizures is expected to be high in elderly people owing to the high prevalence of both epilepsy and RBD in old age. Taking hint from recently observed such association in two elderly people (3), we are performing a systematic investigation about the occurrence of RBD in elderly epilepsy patients and about the prevalence of EEG IEA in elderly people affected with cryptogenic RBD.

Here we are reporting preliminary findings in 10 subjects in whom the coexistence of epileptic seizures or EEG IEA, resulted to be confounding factors in diagnosing RBD. In five men (mean age 71.6 years, range 61–77) all with recent occurrence of cryptogenic sleep-related tonic-clonic seizures (four cases) or of focal onset tonic-clonic seizures during wakefulness (one case), sleep interview revealed the coexistence of nocturnal episodes of “enacted dream” which proved to be episodes of RBD at nocturnal video-polysomnography. RBD predated the occurrence of epileptic seizures by years, were not responsive to antiepileptic drugs whilst showed good response to clonazepam at low doses. In five non-epilepsy subjects (four men and a woman; mean age 66.5 years, ds 7.5) referring for nocturnal episodes of “enacted dream”, the diagnosis of RBD was at first uncertain owing to the presence of epileptiform abnormalities focused on the fronto-temporal areas, at routine EEG. Nocturnal video-PSG led to a definite diagnosis of REM Behavior Disorder in all the cases. Occurrence of IEA in subjects with RBD
should be evaluated cautiously and not interpreted as evidence of epilepsy. In elderly people with epileptic seizures the co-existence of RBD episodes should be taken into consideration.


O 069
Frequency of REM Sleep Behavior Disorder in a mixed sleep disorder population

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Aim: The aim of this study was to examine the frequency of idiopathic and symptomatic REM Sleep Behavior Disorder (RBD) in a mixed sleep disorder population.

Methods: All reports from polysomnographies (PSG) performed between March 2003 and December 2004 at the sleep laboratory of the department of Neurology, Innsbruck Medical University, were reviewed. From a total of 817 polysomnographic reports, 114 were excluded because of multiple examinations during the study period. The polysomnographic reports of 703 patients were entered into the study. RBD was diagnosed according to the International Classification of Sleep Disorders (ICSD) criteria (1). The diagnosis “suspected RBD” or “possibly beginning RBD” was given to patients who had a combination of increased tonic or phasic chin and/or extremity muscle activity during REM sleep, and potentially harmful sleep behaviors (video documented or in the history) when the findings were not definitively conclusive (e.g. only moderately increased phasic muscle activity, or only one potentially harmful sleep behavior in the history).

Results: The study collective consisted of 703 patients (501 men (71.3%) and 202 women (28.7%)) with a mean age of 51.0 ± 14.1 (10–82) years (mean ± standard deviation; range). A diagnosis of definite RBD was given to 19 patients (2.7% of the whole sample; 17 men and 2 women). Out of these, 16 had symptomatic RBD (8 associated with Parkinson’s disease; 1 with multiple system atrophy (MSA); 3 with narcolepsy; 3 drug induced: (1 fluoxetine; 2 venlafaxine); 1 after pontine infarction). 3 patients had idiopathic RBD (one of them had been treated with paroxetine until one week before PSG). A further 16 patients (2.3% of the whole sample, 5 women and 11 men) were given the diagnosis suspected or possibly beginning RBD. In those, 11 patients had a possibly symptomatic etiology of beginning or suspected RBD (3 Parkinson’s disease; 1 narcolepsy; 6 drug induced (3 selective serotonin reuptake inhibitor-SSRI; 3 beta-adrenergic blockers); 1 possibly symptomatic secondary to brain tumor). 5 had a possibly idiopathic etiology.

Conclusion: In this large sleep laboratory patient collective only a small proportion of patients (2.7%) had definite RBD, overwhelmingly due to symptomatic etiology. Men were more frequently affected than women. A further proportion of patients (2.3%) were diagnosed as suspected or possibly beginning RBD. Follow up studies will show if they develop full blown RBD and/or a neurodegenerative disease.

Reference

O 070
REM Sleep Behavior Disorder(RBD) observed in MSLT in a Parkinsons patient

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Aim: To report RBD in a daytime nap in Multiple Sleep Latency Test in a Parkinson’s disease patient.

Methods: We report a 51-year-old male with 4 yr history of Parkinson’s disease who started experiencing daytime sleepiness 2 years ago. His sister reported that sometimes during afternoon naps he flayed his arm and legs and executed movements, as if he was acting out of his dream. The patient does not remember any dreams at that time. He reported dreaming at night. He has been observed by the sister to act out his dream also at night.

Results: We did a polysomnogram followed by MSLT on this patient. On the sleep study there was no REM sleep. He had moderate sleep apnea indicated by an RDI of 20.3/hr. The MSLT showed a sleep latency of 5 min., which indicated excessive sleepiness. There were 4 SOREM periods in the 4 naps carried out. In the first nap during REM sleep the patient was moving his arms to pick something from his body. At the end of the nap the patient reported that he was dreaming of leeches on his body and was trying to remove them. It appears that he was acting out the dream.

Conclusions: RBD is a well-known association with Parkinson’s disease and in about one third of the patients RBD precede the onset of Parkinson’s disease. We report the occurrence of the same phenomenon in the daytime nap when the patient was acting out his dreams. To our knowledge the occurrence of RBD in a daytime nap in MSLT has not been described before.
Epilepsy in Sleep

O 071
The effect of vagus nerve stimulation with different settings on sleep-related breathing in patients with epilepsy

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Aims: Preliminary studies showed that treatment with vagus nerve stimulation (VNS) affects respiration during sleep (Marzec et al. 2003, Mark et al. 2003). We describe the influence of VNS with standard-mode and rapid-cycling-mode on sleep-related breathing in two epilepsy patients.

Methods: In two male epilepsy patients (patient 1 was 35 and patient 2 36 years old) treated with VNS three nights with digital polysomnography (PSG) were performed. Both patients underwent one night without VNS, one night on standard-mode (impulse duration of 30 seconds, impulse frequency every 5 minutes) and a third PSG on rapid-cycling-mode (impulse duration of 7 seconds, impulse frequency every 30 seconds) of VNS. The PSGs were recorded and scored in 30 second epochs according to standard criteria (Rechtschaffen and Kales, 1968). Respiratory monitoring consisted of nasal and buccal airflow (thermocouple) and nasal pressure cannula, tracheal microphone, thoracic and abdominal respiratory effort (Piezo), finger oximetry and electrocardiogram.

Results: Patient 1 had symptomatic epilepsy. He was since 2000 treated with VNS and additionally with levetiracetam 3000 mg, barbexacon 400 mg, carbamazepine 1650 mg. Patient 2 had simple partial seizures, complex partial seizures and secondary generalized seizures, since 1998 treated with VNS and additionally with levetiracetam 3000 mg and phenytoin 600 mg. In the night without VNS patient 1 showed a respiratory distress index (RDI) of 11.9 per hour (/h) and oxygen distress index (ODI) of 10.2 per hour (/h) and therefore a mild sleep disordered breathing in the night with standard-mode of VNS RDI 11.3/h and ODI 5.5/h and in the night with rapid-cycling-mode of VNS RDI 39.4/h and ODI 10.3/h. Patient 2 had RDI 3.4/h and ODI 0.4/h in the night without VNS, RDI 7.9/h and ODI 2.9/h in the night with standard-mode of VNS and RDI 68.1/h and ODI 0.7/h in the night with rapid-cycling-mode of VNS.

Conclusions: Our two case reports confirm data of previous studies, that VNS affects respiration during sleep. A close relationship was found between the vagus nerve stimulus and hypopnea without relevant oxygen desaturation in both patients. The increased number of hypopneas during the night with rapid-cycling-mode of VNS might be related to the higher impulse frequency and cause the decline of RDI without significant deterioration of ODI.

O 072
Ring Chromosome 20 Syndrome: sleep polygraphic recordings

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Objective: Ring chromosome 20 (r20) mosaicism is associated with drug-resistant epilepsy, behavioral disturbances and mild mental retardation, without significant dysmorphism. First reported in 1972 by Atkins et al, over 30 cases have been published since then. Augustijn et al have reported four children with subtle nocturnal frontal lobe seizures. None of these papers describe sleep characteristics or structure, or interictal/ictal discharge distribution during sleep. We studied two patients to determine these features.

Patients and Methods: We studied two female patients whose seizures began during adolescence as non-convulsive status epilepticus (NCSE). These were later accompanied by complex partial seizures with terrors and in one case hallucinations, always before the onset of sleep. Both patients presented behavioral disorders, aggressive behavior, worry and cognitive disorders. Their study included cytogenic analysis, video-EEG monitoring, video-polysomnography (VPGS) and brain MRI.

Results: We found interictal EEG abnormalities of fronto-temporal origin in both cases. The video PSG showed spike and slow-wave discharges which were predominantly fronto-temporal during drowsiness and practically continuous during NREM sleep, and which disappeared in REM sleep and on waking. These features are reminiscent of those reported in the ESES. Cyclic sleep structure is preserved and the graphoelements which define the different phases, spindles and K complexes, were scarce. In both patients we recorded over 30 electroclinical seizures accompanied by motor automatisms and autonomic manifestations in clusters during NREM sleep.

Conclusions: Video-PSG recordings are mandatory in r20 due to the circadian distribution of seizures and behavioral disturbances with predominance in the evening and at sleep onset.

Interictal and ictal paroxysmal activity (motor seizures with automatisms) is NREM-REM sleep-dependent. Sleep electroclinical features could be a phenotypical marker.

O 073
Unusual clinical presentation of nocturnal frontal lobe epilepsy

Siddiqui F., Wei M., Walters A., Chokroverty S.
Objective: To describe an unusual presentation of nocturnal frontal lobe epilepsy.

Methods: 53 year old right-handed male presented with unusual movement episodes since teenage. These episodes were described as flailing of the limbs on both sides of the body with no loss of consciousness, urinary incontinence or tongue bite. His wife notices twisting and turning of the right upper extremity after which he starts having twisting movements of both upper and lower extremities. The episode would last 15 seconds to approximately one minute. The patient would be conscious and oriented during the process. An initial 24-hour EEG was normal. A video polysomnogram and 72 hour Video EEG were recorded.

Results: Video polysomnogram with seizure montage showed 3–4 episodes when the patient aroused from stage 2 sleep and was moving his hand and rubbing his eyes in a stereotypical manner. This happened 4 times during the night with both hands. Each episode lasted 30 seconds. In the later part of the night, he had one episode with ballistic movements of both legs lasting for 45 seconds. The same movements of rubbing eyes with hands were also observed during 72 hour video EEG which lasted 30 seconds. There were no apparent epileptiform discharges in the EEG. These episodes were manifestation of frontal lobe epilepsy and were previously mistaken for pseudoseizures.

Conclusion: Frontal lobe epilepsy has various motor manifestations like tonic, clonic, bipedal, bimanual, and bicycling movements; motor and sexual automatisms; contralateral dystonic posturing or arm abduction with or without eye deviation. Rubbing eyes with hands is yet another unusual manifestation of Frontal lobe epilepsy which to our knowledge has not been described before.

O 074
Sleep disorders in ADHD children.

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A high prevalence of RLS and/or PLMs has been already documented in ADHD or well as comorbidity with focal seizures. We recorded over night a sample of 11 male, ADHD children, mean age 9.3 (age range 4–13). Video-polisomnomography included a minimum of 8 to a maximum of 16 leads (in children who had previously displayed epileptic abnormalities on day-time EEG) with 21 electrodes (10–20 system).

Sleep was altered in 10/11 children. 7 patients had diagnostic PLMs indexes (mean 29.2, range 12–52), 4 qualified for RLS. Disorders of arousal (DOA) were recorded in 4 children. Enuresis, bruxism and snoring with SBD were recorded in 2 patients each.

Focal interictal abnormalities were detected in 8/11 children: centro-temporal bilaterally (rolandic) in 4 patients, bifrontal with left predominance in 2, left anterior temporal in 1, right occipital in 1. 2 children had nocturnal focal seizures (rolandic and occipital) during recording.

Levetiracetam (250 mg to 1000 mg depending on body weight) was started either with single night dosing or with double dosing (in the presence of seizures), in all children with DOAs, RLS, PLMs and seizures. DOAs and seizures both subsided in a 3–8 month follow-up, while PLMs improved with decreased sleep discontinuity in patients with RLS and/or PLMs. Instrumental (all night polysomnography) is currently being repeated in all subjects for objective reevaluation following therapy.

O 075
Arousal Duration is Less as a Function of Age during Active Sleep in Preterm Infants Compared with Full-term Infants from the Collaborative Home Infant Monitoring Evaluation Study Database.

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Aims: Preterm (PT), and full term (FT) infants, during the first two to four months, have greater risk for Sudden Infant Death Syndrome (SIDS) in part due to immaturity of sleep and arousal. These are studies using the archived digital recordings to analyze sleep and arousal characteristics from the Collaborative Home Infant Monitoring Evaluation (CHIME) study infants.

Methods: We have obtained the archived polygraphic records of 555 infants from the CHIME national study database. The digital CHIME polygraph data were converted to European Data Format and were visually scored for sleep and spontaneous arousal using Somnologica. Overnight records at term post menstrual age (PMA) or at 3 mon PMA age from ten PT and 8 FT infants were scored for quiet (QS), active (AS) and indeterminate sleep (IS) using standard polygraphic criteria. Video recordings were not available. During sleep, episodes ranging from 3 to 60 s, with increased heart rate pattern change (more than 2SD above baseline:
Sleep in young Prader Willi Syndrome patients. Can we maintain the narcolepsy hypothesis?

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Phasic EEG events characterize the so-called “sleep microstructure” which, during non-REM sleep, shows a peculiar organization, indicated as “cyclic alternating pattern” (CAP). CAP translates a condition of sustained arousal instability oscillating between a high (phase A) and a low level (phase B). The aim of this study was to analyze the intervals between subsequent CAP A phases and to discover their eventual time interdependency. Two groups of normal subjects, adults and children, were used for this study; each subject underwent 1 polysomnographic night recording and sleep stages were scored before the detection of each CAP A phase. First, we analyzed the histograms of distribution of intervals between subsequent CAP A phases and, subsequently, we analyzed their time structure by means of a
Markovian analysis. The comparison between the interval distribution graphs obtained from light sleep (LS) and slow-wave-sleep (SWS) in children showed a statistically significant difference for intervals \( \geq 10 < 20 \) s, higher during SWS, and for intervals \( \geq 55 < 60, \geq 95 < 100, \) and \( \geq 120 < 125 \) s, slightly higher during LS. The interval distribution graphs obtained from children and adults during LS were substantially similar; during SWS we found significant differences with interval classes \( \geq 5 < 15 \) and \( \geq 70 < 75 \) s higher in children and intervals classes \( \geq 20 < 30 \) and \( \geq 35 < 40 \) s higher in adults. The Markovian analysis disclosed that the entropy of the CAP interval dynamics during SWS was significantly different between the two groups, with lower values in adults. The comparison between LS and SWS in children disclosed a significant difference with entropy values higher during SWS than during LS. The same was found for the adult group. All these results show that there is a deterministically generated time structure of the arousal fluctuations during sleep which might be driven by external sensory inputs but autonomously predispose the brain to be less or more influenced by the environment.

**O 078**

**Micro-environment and sleep behaviour in the infants**

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The study aimed at assessing possible relationship between the quality of infant environment and maternal reported behavioural features during sleep in 2-month-old infants. It comprised 115 randomly selected, apparently healthy infants (50 boys, 65 girls) from community setting who were singletons born at term with normal birth weight in St. Petersburg in 2001–2002. Quality of infant care was estimated using the “PROCESS” (Paediatric Review of Children’s Environment Support and Stimulation) inventory enabling to measure infant’s developmental stimulation and organisation. Infant’s behaviour during sleep was assessed using an adapted version of the Children’s Sleep Habits Questionnaire (CSHQ). The babies facing more developmental stimulation and from more organised environment less often fell asleep in parents bed (\( P = 0.036 \)). Infants from more organised environment were more often put to sleep at the same time at night, more often were ready to go to sleep at bedtime and less often struggled at bed; it was more common with them to have right amount of sleep and to have about a same amount of sleep each day; less often they moved a lot during sleep and woke up in sleep. These associations remained significant after adjustment has been made for each of such potential confounders as infant’s gender, weight at birth and at study, gestational age, Apgar score at 1 and 5 minutes, birth order, maternal age and education, maternal marital status, infant’s feeding at birth and at study, as well as to their simultaneous effects. Lower environmental organisation and developmental stimulation may be associated with specific disadvantageous infant behavioural features during sleep. Infants with parentally reported sleep problems should be carefully considered for possible flaws in the quality of environment.

**O 079**

**Sleep Cyclic Alternating Pattern in Children with Mild Sleep-Disordered Breathing**

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*Introduction: Sleep-disordered breathing (SDB) in children can cause behavior changes and cognitive deficits, including hyperactivity, inattention, and sleepiness. Cyclic alternating pattern (CAP) is a marker of sleep instability, and it can be a good parameter for disrupted nocturnal sleep in patients with mild sleep disorders. We hypothesized that CAP would be abnormal in children without sleep apnea syndrome but chronic snoring and daytime symptoms.*

*Methods: We selected 15 children with an apnea-hypopnea index (AHI) < 2/hours, absence of SaO\(_2\) drop > 2% during night. Control group were matched with patient group in age, Tanner stage and gender measures. All subjects had clinical evaluation and polysomnography. The following variables were monitored: EEG, EOG, chin and leg EMG, EKG. Respiration was monitored with nasal cannula/pressure transducer, oral thermistor, neck microphone, pulse-oximetry, chest and abdominal belts, intercostal EMG, esophageal pressure sensor. Sleep was analyzed following Rechtschaffen and Kales and American Sleep Disorder Association criteria, adding CAP measures following Terzano et al. recommendations.*

*Results: The parents of children complained of hyperactivity, impulsivity, and depressed mood in 75% of our patient group. All patients were chronic heavy snorers. They presented an AI = 0, RDI = 10.2/h and with a lowest SaO\(_2\)Hb = 98.1(2.4)%. None of them responded to the obstructive sleep apnea syndrome (OSAS) criteria but fitted the diagnosed of UARS. No differences were found with conventional scoring. Patients presented a significant increased in CAP rate compared to controls (65.2(6.6)% vs 52.8(8.6)% (U-test, \( p < 0.01 \)), and a significant increase in CAP during slow wave sleep (94.3(1.6)% vs 83.0(2.6)% (U-test, \( p < 0.01 \)).

*Conclusion: Children with chronic snoring who do not respond to the criteria for OSAS present an abnormal sleep
EEG with a significant increased in CAP rate, with a predominance of abnormalities in slow wave sleep.

Support: Dr. MC Lopes is supported by an educational grant from SANOFI-AVENTIS.

O 080
Sleep habits and consequences of disordered sleep in healthy school children in a developing country

Mustafa G., Bukhari S. K. A., ul Haq A., Hussain Z.
Children Hospital Complex, Multan, Pakistan

Relatively less data, currently, exists concerning the sleep habits and the consequences of disordered sleep in school children of the developing countries. This descriptive study examined a variety of common sleep habits and problems in a group of 4896 elementary school children from grades kindergarten to tenth. A battery of parent reported sleep questionnaires, concerning sleep habits and problems, was developed. The schools were randomly selected from an urban area. The parents reported 12% children sleeping poorly and 2% of children relied on sedatives to induce sleep.

Sleep difficulties lasting more than 4 months were present in 23% of the children. Younger children were more likely than older children to have sleep problems noted by parents (particularly bedtime struggles and night time waking). In 6%, sleep latency was longer than 45 minutes, and more than one complete arousal occurred during the night, at least once per month.

The following variables were seen among the poor sleepers: low parental education, higher socioeconomic status, higher professional status, while noise or light in the rooms they slept, were not a problem for these children.

Predominance of abnormalities in slow wave sleep.

O 081
Clinical and polysomnographic evaluation in infants at risk for Apparent Life Threatening Event (ALTE)

Nosetti L.1, Castronovo V. E.2, Gandini V.1, Favaro S.1, Veronelli E.1, Loda B.1, Salvatore S.1, Nespoli L.1, Ferini-Strambi L.2

O 082
Variability of the Hypoxic Ventilatory Response in Sleeping Infants

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Introduction: Infant with an ALTE present to medical attention because of an acute unexpected change in behaviour reported as life-threatening (that occurs during sleep, awake or feeding). Up to 50% of all ALTE remained unexplained (idiopathic). Recurrent ALTE have been associated with obstructive sleep apneas, digestive, neurological abnormalities and metabolic disorders. A multidisciplinary approach is highly recommended. Altered autonomic function, reduced arousability, increased respiratory effort, obstructive sleep apnea, frequent episodes of hypoxemia have been suggested as markers. The PSG evaluation may be important in particular in the idiopathic form. Aim of our study was to investigate wheter anamnestic information and objective data (pH monitoring, PSG, cardiorespiratory home monitoring) could identify infants at high risk for ALTE.

Methods: In a 4-years period 232 infants (106 F/126 M; median age 68.3 days) who had experience ALTE and 80 age-matched controls were studied. A complete clinical evaluation including information on anthropometric data, family history, exposition to passive smoking, alcohol and drug intake, delivery modality, Apgar score, prematurity, growth, specific circumstances of ALTE episode was performed. Moreover all patients underwent extensive emathological tests, cerebral ecography, ECG and instrumentation monitoring (pH-recording, PSG and cardiorespiratory home monitoring). All collected variables were statistically analysed in order to assess the best predictive risk factors for ALTE.

Results: No significant differences were observed between ALTE infants and controls in total sleep time, delay in sleep onset, time of awake, % of REM and nonREM sleep, number and duration of apneas. The major risk factors resulted: gastrointestinal disease (p < .001), smoking in pregnancy (p < .001), previous ALTE (p < .0001), reflux index and number of refluxes measured by pH monitoring (p < .001), Apgar 1 and 5 score (p < .005) and type of delivery (p < .005).

Conclusion: Our results confirmed that a detailed anamnestic evaluation as well as objective evaluations are important for detecting infants at high risk for ALTE. The further evaluation of polysomnographic data and in particular of the autonomic nervous system functioning may give important indication both on the pathogenesis of this phenomena and on its management in order to contribute to the care of this common condition.

O 080
Sleep habits and consequences of disordered sleep in healthy school children in a developing country

Mustafa G., Bukhari S. K. A., ul Haq A., Hussain Z.
Children Hospital Complex, Multan, Pakistan

Relatively less data, currently, exists concerning the sleep habits and the consequences of disordered sleep in school children of the developing countries. This descriptive study examined a variety of common sleep habits and problems in a group of 4896 elementary school children from grades kindergarten to tenth. A battery of parent reported sleep questionnaires, concerning sleep habits and problems, was developed. The schools were randomly selected from an urban area. The parents reported 12% children sleeping poorly and 2% of children relied on sedatives to induce sleep.

Sleep difficulties lasting more than 4 months were present in 23% of the children. Younger children were more likely than older children to have sleep problems noted by parents (particularly bedtime struggles and night time waking). In 6%, sleep latency was longer than 45 minutes, and more than one complete arousal occurred during the night, at least once per month.

The following variables were seen among the poor sleepers: low parental education, higher socioeconomic status, higher professional status, while noise or light in the rooms they slept, were not a problem for these children.

Approximately 5% of the sample was identified as having significant problems with daytime sleepiness. The insomniac fathers were a significant factor (P < .001) for boys who slept poorly. The 37% of “poor sleepers,” had failed 1 or more years at school. It is noted that achievements were significantly difficult to attain by the poor sleepers than among the children without sleep problems (P = .001). Only 10% of parents were desirous of seeking any medical advice for their children’s sleep problem.

The results of this study emphasize that different factors operate and influence the sleep habits and it’s consequences in the developed and the developing countries.

O 081
Clinical and polysomnographic evaluation in infants at risk for Apparent Life Threatening Event (ALTE)

Nosetti L.1, Castronovo V. E.2, Gandini V.1, Favaro S.1, Veronelli E.1, Loda B.1, Salvatore S.1, Nespoli L.1, Ferini-Strambi L.2

O 082
Variability of the Hypoxic Ventilatory Response in Sleeping Infants

1Dept of Pediatrics, University Insubria, Varese, Italy and 2Sleep Disorders Center, University Vita-Salute San Raffaele, Milano, Italy

Introduction: Infant with an ALTE present to medical attention because of an acute unexpected change in behaviour reported as life-threatening (that occurs during sleep, awake or feeding). Up to 50% of all ALTE remained unexplained (idiopathic). Recurrent ALTE have been associated with obstructive sleep apneas, digestive, neurological abnormalities and metabolic disorders. A multidisciplinary approach is highly recommended. Altered autonomic function, reduced arousability, increased respiratory effort, obstructive sleep apnea, frequent episodes of hypoxemia have been suggested as markers. The PSG evaluation may be important in particular in the idiopathic form. Aim of our study was to investigate wheter anamnestic information and objective data (pH monitoring, PSG, cardiorespiratory home monitoring) could identify infants at high risk for ALTE.

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Conclusion: Our results confirmed that a detailed anamnestic evaluation as well as objective evaluations are important for detecting infants at high risk for ALTE. The further evaluation of polysomnographic data and in particular of the autonomic nervous system functioning may give important indication both on the pathogenesis of this phenomena and on its management in order to contribute to the care of this common condition.
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**Aims:** Previous studies of infants exposed to hypoxia have reported an immature biphasic response consisting of an initial increase followed by a reduction in ventilation. These studies of the hypoxic ventilatory response (HVR) have primarily been conducted in quiet sleep (QS) alone and furthermore, few studies have made repeated measurements in the same infant. Our aim was to gain a more complete knowledge of the maturation and consistency of the initial phase of the HVR in human term infants in both quiet and active sleep (AS), by performing multiple tests longitudinally across the first 6 months of life. We hypothesised that sleep state would have a marked effect on the HVR and that a significant maturation would be observed.

**Methods:** Fifteen healthy term infants, born at 38–41 wk gestational age, were studied with daytime polysomnography longitudinally at 2–5 wk, 2–3 mo and 5–6 mo after birth. Nasal airflow was measured using a miniaturised pneumotachograph attached to a silicone rubber nose-mask. Each infant was challenged with hypoxia (15% O2, balance N2) in both AS and QS. Tests were terminated if (a) the infant aroused, (b) after 5 minutes with no arousal, or (c) if SpO2 fell below 85%. Mean values of oxygen saturation (SpO2) and inspired minute ventilation (V'I (mL/min/kg)) were calculated for 15 s epochs over the initial 30s of the test, and expressed as percentage changes relative to baseline values. Data from tests repeated within each infant were averaged for each sleep state; arousing and non arousing tests were analysed separately. The effects of sleep state and postnatal age on the variance in each group were compared using the F-test.

**Results:** In AS infants consistently aroused; however, in QS infants both aroused and failed to arouse in response to hypoxia. At each age, a significant decrease in SpO2 occurred in both sleep states, regardless of arousal. The initial HVR, varied considerably between infants, with V'I/kg either increasing, decreasing, or exhibiting not changing. The HVR was markedly more variable during AS compared with QS at all three ages (p<0.05). Variability decreased with postnatal age in both sleep states (p<0.05); however in QS tests which failed to induce arousal, variation between infants was lowest at 2–3 mo (p<0.05).

**Conclusions:** This study has demonstrated that the initial phase of the HVR varies between term infants during both AS and QS. In support of our hypothesis, the response was markedly more variable during AS, and became more consistent with increasing postnatal age. By performing only one test or by failing to account for arousal responses, previous studies may not have detected the natural variation of the infant HVR.

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**O 083**

A comparison of actigraphy and sleep diaries to determine the maturation of infant sleep over the first year of life

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**Aims:** Maturation of sleep/wake patterns is one of the most important physiological developments during the first year of life. To date there have been few longitudinal studies to evaluate the development of normal infant sleep patterns. In this study we aimed to quantify infant sleep/wake patterns in the home over the first year of life using a combination of actigraphy and sleep diaries.

**Methods:** Twenty healthy term infants (7F/13M) were recruited and studied for 3 days each month in their own homes over the first 12 months of life. Sleep/wake patterns were recorded using both sleep diaries and actigraphy (AW64, Mini Mitter Co Inc Sunriver OR USA). The development of sleep and wake was analysed over 24 hours, during the day (08:00–20:00) and during the night (20:00–08:00). Data were compared between methods at each age with paired Students' t-tests and across ages with ANOVA.

**Results:** 186 studies had complete data sets for both analysis methods. Overall there was no difference between methods of measurement for determination of the total % of sleep or wake over 24 hours, or for the total % of sleep or wake during the day. However, at night, actigraphy scored less time asleep (73.3 ± 0.9%) and more time awake (26.7 ± 0.9%) compared with the sleep diaries (80.7 ± 1.04% and 19 ± 1.0% respectively, p<0.001). Mean % sleep during the day decreased from 51% at one month to 28% at 12 months with the one month values being significantly higher than all other ages, while mean % sleep at night was only different between 1 month and 11 and 12 months. Sleep diaries showed no difference across the 12 months in total % sleep over 24 hours, however actigraphy showed more total % sleep at 1 month than at any of the other ages.

**Conclusion:** Actigraphy may provide a useful tool for assessing infant sleep, however further studies using video recording to validate these findings need to be carried out. Supported by the Bonnie Babes Foundation, Karitane and the Clive and Vera Ramaciotti Foundation.

**Mental disorders/Psychiatric/Personality**

**O 084**

Visuospatial abilities and sleep-dependent EEG oscillations: frequency- and region-specific correlations

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Aims: The cerebral cortex is a major modulator of sleep electroencephalogram (EEG) oscillations, and the latter were shown to reflect corticothalamic resonance as well as synaptic plasticity and neural transmission efficacy phenomena. There is evidence for a sleep-EEG alteration in various forms of dementia as well as for a correlation between certain sleep-EEG features and cognitive performances in normal non-demented subjects. Our aim was to detect sleep-EEG based biomarkers of low visuospatial ability in normal non-demented subjects. We hypothesized that individual differences in the sleep-slow oscillation as well as in slow- and fast sleep spindle activity reflect visuospatial memory ability in a region- and frequency-specific manner.

Methods: Nineteen subjects slept two consecutive nights in the sleep laboratory (EEG: 10–20 system, polygraphy: submental EMG, left- and right EOG, ECG). The immediate (3 minutes) and delayed (30 minutes) recall as well as the recognition trial of the Rey-Osterrieth Complex Figure Test was used for assessing individual differences in visuospatial memory ability. An individual adjustment of frequency and amplitude criteria of slow- and fast sleep spindling was used in sleep spindle analysis and detection.

Results: Here we report negative correlations of visuospatial recall performance with integrated relative amplitude spectra of slow spindle frequency activity. Moreover, positive correlations between visuospatial recall performance and right parietal fast spindle density as well as visuospatial recognition performance and the integrated amplitude spectra of fast spindle frequency activity in the right centroparietal area were observed. Neither the sleep-slow oscillation, nor the grouping of slow or fast sleep spindles by the slow oscillation correlated significantly with visuospatial abilities.

Conclusions: Results suggest that slow spindle frequency activity is a global, region-independent, negative biomarker of visuospatial memory ability, while region-specific differences in fast sleep spindle activity and density are correlates of the neuropsychological performances associated with the respective regions. Stable individual differences in functional neuroanatomy and cortical connectivity may shape both sleep-EEG oscillations and visuospatial memory ability.

O 085
Delta power in sleep and neuropsychological performance in patients with schizophrenia and healthy controls
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Aims: Recent studies reported on associations between delta power in sleep and performance at neuropsychological tests. This link might be altered in schizophrenia because of a decrease of delta power in sleep on the one hand and pronounced cognitive deficits on the other hand.

Methods: We therefore analysed delta power in sleep in 16 patients with schizophrenia (ICD 10) on stable antipsychotic medication with amisulpride (age range 22 to 44 years) and 17 healthy controls. Immediately before polysomnography and the morning after we performed different neuropsychological tasks including Trail Making Test parts A and B, Rey-Osterrieth Complex Figure Test, a mirror tracing skill and the Tower of Hanoi.

Results: In healthy subjects we found significant positive correlations between performance in attention, cognitive flexibility and memory skills and delta power. In comparison to healthy controls, the patients with schizophrenia showed a decrease in delta power in SWS and altered correlations between test performances and delta power.

Conclusions: These results point to a functional interrelationship between delta power in sleep and cognitive performance in healthy subjects and to alterations of this link in patients with schizophrenia.

O 086
Cyclic Alternating Pattern in patients with major depressive disorder treated by a novel agent: Agomelatine
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Introduction: Depressive episodes are common health problem, often linked with disturbed sleep. Moreover, several studies have described the quality of sleep in depressive disorders as an important marker of response to treatment and risk of recurrence. However, the conventional scores of sleep patterns are limited in evaluation of sleep during treatment of patients with major depressive disorder (MDD). Cyclic alternating pattern (CAP) is a marker of NREM sleep stability, and it can be a new approach in MDD patients. Agomelatine is the first melatonergic antidepressant presenting an innovative pharmacological profile: it is an agonist at MT1 and MT2 receptors with 5-HT2C antagonist properties. Agomelatine 25 mg per day has been shown to be effective in MDD without affecting daytime alertness. The purpose of the study was to assess...
the effect of agomelatine 25 mg on sleep architecture using CAP analysis in outpatients suffering from MDD.

Methods: 15 out-patients with a major depression episode (DSM-IV), aged between 20 and 56 years, with a baseline HAM-D score ≥ 20 received agomelatine 25 mg p.o. a day for 42 days. Polysomnography was performed at D-1 (adaptation night), D0, D7, D14, D41 (adaptation night) and D42.

Wake and sleep staging were analysed by the Rechtschaffen and Kales international criteria. A CAP analysis was performed with investigator blind to patient’s condition following the international atlas recommendations.

Results: The CAP parameters indicated very important changes that were even more marked than those noted with conventional sleep scoring. The CAP rate, CAP time and CAP cycle were decreased comparing baseline night to treatment nights 7 and 42, respectively: CAP rate went from 61.5(5.9) to 32.9(11.1) and 30.1(10.7)%; CAP time changed from 205.7(45.9) to 84(26.7) and 84.8(40.8) minutes; finally the number of CAP cycle went from 444.9(82.1) to 173.0(58.1) and 177.0(87.4). All baseline results were significantly different from treatment nights, but no difference was seen between the 2 treatment nights (ANOVA (p=0.0001), with post hoc analysis with tukey test (p=0.05) baseline versus night 7 and night 42). A phase A subtype analysis was also performed:

<table>
<thead>
<tr>
<th>(%)</th>
<th>Baseline</th>
<th>Night 7</th>
<th>Night 42</th>
<th>p-value (ANOVA) post-hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1 subtype</td>
<td>47(9)</td>
<td>60(16)</td>
<td>65(14)</td>
<td>0.0002 B &lt; N7, N42</td>
</tr>
<tr>
<td>A2 subtype</td>
<td>33(6)</td>
<td>23(13)</td>
<td>21(13)</td>
<td>&lt;0.0125 B &gt; N7, N42</td>
</tr>
<tr>
<td>A3 subtype</td>
<td>19(7)</td>
<td>13(9)</td>
<td>13(6)</td>
<td>&lt;0.0125 B &gt; N7, N42</td>
</tr>
</tbody>
</table>

As can be seen, there was a significant decrease in phase A2 and A3 (p=0.05 Tukey test post ANOVA) and a significant increase in phase A1 (p=0.05 post hoc Tukey test) with medication.

Conclusions: Our results showed that agomelatine brought a significant and very early improvement (night 7) in sleep quality. CAP came out to be a very useful tool in evaluating the impact of antidepressant treatment on sleep in patients with MDD.

O 087
A new data acquisition system for monitoring circadian variations of activity and ECG: Clinical application

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O 088
Sleep Disturbances are Common in Hemodialysis Patients and are Associated with a Poor Quality of Life: A Case Controlled Study

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This case controlled study was performed to assess the prevalence of sleep complaints, to characterize specific sleep disorders and their effect on quality of life in hemodialysis patients awaiting renal transplantation. Seventy five patients and an equal number of age and sex matched control subjects were assessed by three questionnaires: Sleep and Health Questionnaire (SHQ) and Epworth Sleepiness Scale (ESS) were used to evaluate sleep disturbances, while Medical Outcomes Survey SF-36 was used to assess the quality of life. Polysomnography (PSG) was performed in 29 unselected patients. There were 61 males and 14 females. The mean age of the patients was 36.9 years. The body mass index of patients was significantly lower than that of the controls (20.61 + 3.38 vs 22.88 + 3.22), although their waist/hip ratio and neck circumference were similar. The patients were adequately dialysed and the mean dialysis duration was 4.5 months. The prevalence of co-morbidities amongst patients was low (mean 0.41). Sleep complaints were present in majority of patients (74%) and were significantly higher in patients than in controls (p<0.01). Excessive day time sleepiness, sleep onset insomnia and sleep maintenance insomnia were the commonest symptoms present. There was no correlation between sleep complaints and age, gender or duration of dialysis. Restless legs syndrome (RLS) was present in 14% of the patients (controls 4%). Symptoms of RLS contributed to sleep onset insomnia and sleep maintenance insomnia. PSG confirmed that sleep disordered breathing and obstructive sleep apnoea (OSA) were present in 24% and 17.3% of patients respectively. Central sleep apnoea was present in 13.8% of the patients assessed by PSG, while Periodic leg movements disorder was present in 20.6%. Prevalence of sleep complaints and RLS were associated with limitation of physical and mental abilities assessed in the various domains of SF-36. We conclude that sleep complaints were prevalent in majority of our hemodialysis patients; with excessive daytime sleepiness, sleep onset insomnia and sleep maintenance insomnia being the most common complaints. Specific sleep disorders such as OSA and RLS were also more prevalent than in controls. Quality of life was poor in patients with sleep disorders.

O 089
Sleep Misperception in Patients with Rheumatoid Arthritis

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Difficulty initiating and maintaining sleep (insomnia) is often reported by patients with rheumatoid arthritis (RA). Polysomnography (PSG) has shown normal sleep architecture, total sleep time (TST), and sleep latency (SL) despite sleep fragmentation (arousal index, AI), with extremity movements (PLMs) and prolonged wake after sleep onset (WASO). Patient self-reported (PSR) sleep parameters suggested a substantial Sleep Discrepancy (SD) similar to sleep misperception reported in patients with idiopathic insomnia.

Methods: We recruited 13 RA patients for a series of sleep studies (140 PSGs) before and after randomized, double blind, one month treatments with 6 medications* selected to alter SL, TST, AI, PLMs, WASO and pain. Sleep Discrepancy, as a measure of sleep state misperception, was the difference between PSG and PSR measures.

Results: Baseline PSG data: SL 18 m, TST 394 m, WASO 84 m, AI 33/hr, #wakes 17/night compared to PSR-SL 60 m, PSR-TST 390 m, PSR-#wakes 2.8/night. Drugs did not change SL or TST by PSG. WASO decreased 48% on Codeine(p=.01), AI dec 33% on clonazepam (p<.05), PLMs dec 19% on clonazepam. PSR- SL was unchanged, PSR-TST inc on clonazepam(p<.05) and PSR # wakes dec on indomethacin and carbidopa/L-dopa (p<.05). [* Indomethacin 75 mgSR, Codeine 60 mg, Amitriptyline 25 mg, Carbidopa/L-dopa 25/250, Triazolam .25 mg, Clonazepam 1 mg] 

Table 1 Sleep Discrepancy—a measure of sleep state misperception

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sleep Discrepancy</th>
<th>Number of Wakes/night</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SL</td>
<td>TST</td>
</tr>
<tr>
<td>Baseline</td>
<td>42 (55)*</td>
<td>70 (65)**</td>
</tr>
<tr>
<td>Change with:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indocin</td>
<td>-7</td>
<td>-29</td>
</tr>
<tr>
<td>Codeine</td>
<td>-13</td>
<td>-15</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>0.5</td>
<td>-4</td>
</tr>
<tr>
<td>Carbidopa/L-dopa</td>
<td>.6</td>
<td>-38*</td>
</tr>
<tr>
<td>Triazolam</td>
<td>-4</td>
<td>-11</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>-5.5</td>
<td>-15</td>
</tr>
</tbody>
</table>

*p = .05 **p = .002 ***p < .001

Conclusions: A significant Sleep Discrepancy between PSR and objective PSG measures of sleep was similar to sleep misperception in idiopathic insomnia. This raises serious concerns about the use of patient self-report instruments to measure sleep quantity and quality in clinical research and practice. Large variability within and between individuals on repeated PSG and PSR measures resulted in large standard deviations. Medications tended to reduce sleep discrepancy but changes were significant only with sinemet. These findings suggest the primary effect of ‘sleep inducing’ medications may be to alter the patient’s perception of sleep quality and quantity.

O 090
Psychiatric impact of sleep related breathing disorder and cardiac resynchronisation therapy on patients with chronic heart failure
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Aims: Advanced heart failure often is associated with severe sleep related breathing disorders (SRBD) especially centrally derived forms (30–55%), with reduction of various aspects of quality of life and independent prediction of enhanced mortality [1]. Cardiac resynchronization therapy (CRT) improves central SRBD and sleep quality in patients with severe chronic heart failure (CHF) [2]. However, in the large group of patients with stable CHF the influence of moderate SRBD on sleep, quality of life, and mood as well as the value of cardiac resynchronization therapy (CRT) is not yet established.

Methods: Applying echocardiography, spirometry and ambulatory polygraphy we identified 69 patients with stable CHF (NYHA II-III) either with SRBD (Apnea/Hypopnea-Index: AHI 16–30/h) or without (AHI <5/h) SRBD. Age-matched healthy volunteers and patients with exclusive obstructive sleep apnea (OSAS) served as controls. All participants were evaluated psychometrically for sleep quality (PSQI), mood (BDI) and health related quality of life (SF-36). Furthermore, in patients (24 CHF/SRBD vs. 14 CHF) with conduction disturbances tests were performed before and after (18 ±6 weeks) implantation of CRT.

Results: As opposed to patients with exclusive CHF, severity of additional moderate SRBD correlated with reduction of sleep quality, quality of life and increase of depressed symptoms. While CRT led to improved myocardial function, patients with additional SRBD presented with a decrease of AHI in correlation with improvement of sleep quality, quality of life, and mood: all previous (1/3) symptomatic depressed patients were subjectively non-depressed thereafter.

Conclusion: In stable CHF, comorbidity with even moderate SRBD worsens quality of sleep and life [3], and also correlates with depressed mood; all of these improved by CRT in case of conduction disturbances [4]. SRBD may represent a risk factor for reduced mortality and organic induced (sub-)syndromal depressed states in CHF and should be treated accordingly.

References

O 091
The Influence of Nocturnal Desaturation on Glomerular Filtration Rate in Mild to Moderate Hypertensives

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Background: The prevalence and incidence of end-stage renal disease in patients (pts) with sleep-disordered breathing (SDB) are increasing, but milder renal disease is much more common and may often go undiagnosed and undertreated, although epidemiological studies suggest that, pts with minor impairment of renal function are at higher risk of cardiovascular events, which is observed often in pts with SDB. The aim of this study was to evaluate the possible relationship between the nocturnal desaturation and glomerular filtration rate (GFR) in pts with mild to moderate arterial hypertension (AH).

Methods: We studied 67 (46 male, 21 female, mean age 52±11 year) pts with mild to moderate AH. They underwent non-invasive 24-h blood pressure (BP) and nocturnal arterial oxygen saturation monitoring. 24-h BP recordings (‘TM-2425, A&D’) were performed with intervals of 15 min during the daytime and 30 min during the nighttime. The nocturnal (8 hours) monitoring of arterial oxygen saturation (SaO₂) was performed with pulseoxymeter ‘NONIN 8500M’ and analyzed with original program ‘ARM-SaO₂’. Nocturnal hypoxaemia was assessed by the number of 4% desaturations (DN) from the baseline stable value, during the monitoring. GFR was assessed by measurement endogenous creatinine clearance, which was calculated by the formulae of Cockcroft D. and Gault M. (1976). According by tertile values of DN, pts were divided into 3 groups: Gr.1 (DN<10), Gr.2 (10≤DN<30) and Gr.3 (DN≥30). Differences of estimated parameters (M±STD) between groups were tested by Kruskal-Wallis ANOVA, the relationship between GFR and other variables-by Spearman rank order correlation analysis.

Results: GFR were significantly higher in the Gr.2 and lower in Gr.3 (96±21 vs 113±28 vs 91±23 ml/min, p<0.01). In Gr.3 GFR was significantly correlated with age (r = –0.63, p<0.01), DN (r = –0.51, p<0.01) and were observed a tendency with nighttime PP (r = –0.36, p<0.1). The pts in the Gr.1 and Gr.2 were significantly younger in comparison with Gr.3 (50±10 vs 48±11 vs 58±9 year; p<0.01). There were found no significant differences between groups by body mass index, duration of AH, daytime (D) and nighttime (N) values of systolic and diastolic BP-s. D. and N values of pulse pressure (PP) were significantly higher in Gr.3 (PP(D)-57±14 vs 54±10 vs 63±12 mm Hg, p<0.01 between Gr.2 and Gr.3; PP(N)-52±12 vs 50±10 vs 61±11 mm Hg, p<0.01 between Gr.2 and Gr.3, p<0.01 between Gr.1 and Gr.3).
Conclusion: 1) The number of nocturnal desaturation, as a marker of SDB, is a risk factor for impairment of renal function; 2) The negative association of reduced GFR with nocturnal PP, a correlate of the pulsitile hemodynamic load and conduit vessel stiffness is an important cardiovascular risk factor, and very common in pts with SDB. It appeared that these two unfavorable factors, probably, are additive for target-organ damages leading to cardiovascular events in patients with SDB and AH.

Sleep Health Care Delivery

O 092
Sleepless in America: Treating Insomnia Across the Lifespan

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Sleep takes up one-third of our lives. At least it should. While complaints of insomnia are typically not the precipitating factor for the office visit, patients will reveal their sleeping difficulties when asked a few simple, straightforward questions. Sleep problems are the source of significant co-morbidities. This presentation will provide information about the prevalence, morbidity and diagnosis of insomnia and some tools for behavioral and pharmacological management of this disorder for all age groups.

Epidemiology/Individual Differences

O 093
Sleep Complaints and Sociodemographic Characteristics of the Population of West part of Lithuania

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Aim: was to assess the prevalence of sleep complaints and their relations with sociodemographic characteristics among the citizens of West part of Lithuania.

Methods: Randomly selected 1602 citizens, aged 35–74 years, of Palanga city located in West part of Lithuania were investigated. Sleep complaints and their frequency evaluated by Basic Nordic Sleep Questionnaire (SSRS, 1988). Sociodemographic data was obtained using questions about the family status, education and employment status. Relations among the qualitative variables were evaluated using \( \chi^2 \) criteria. Tests of differences between proportions were used.

Statistical analysis of the data performed using programs STATISTICA and SPSS. All respondents according to subjective sleep quality evaluation (Basic Nordic Sleep Questionnaire) were divided into good (793 subjects) and poor (809 subjects) sleepers’ groups. Good sleepers responded that they had been sleeping well or rather well during the past three months and did not take sleeping pills. Poor sleepers answered that they had been sleeping neither well nor badly, rather badly or badly during the past three months and had used sleeping pills more often than once per month.

Results: Global dissatisfaction of sleep and use of sleeping pills were observed in 50.5 percent of respondents. Poor sleep was more prevalent among females than males (52.8%, 95% CI \( \pm 3.1\% \) vs. 47.2%, 95% CI \( \pm 4.0\% \)) as well as among older than younger respondents (35–44 years: 38.7% vs. 44.0%, 55–64 years: 60.0% vs. 56.2%, \( p < 0.05 \), respectively in males and females). Divorced or widowed females slept worse than living in the family or single ones (respectively 55.5% vs 51.6% vs. 52.1%, \( p > 0.05 \)). Poor sleep was more prevalent among single males than married, living with someone, divorced or widowed (respectively, 54.5% vs. 46.6% vs. 51.0%, \( p > 0.05 \)). Less educated respondents slept worse than those with university education (females: 61.9% vs. 41.1%, \( p < 0.001 \); males: 56.5% vs. 43.6%, \( p > 0.05 \), respectively). Poor sleep was more prevalent among jobless respondents than among those who had job (females: 61.7% vs. 45.9%, \( p < 0.001 \), males: 49.5% vs. 45.9%, \( p > 0.05 \), respectively).

Conclusions: In more than a half of investigated population was found poor sleep which was significantly more prevalent among females, aged, less educated and jobless persons.

O 094
Epidemiological study on relations between OSAS and COPD

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Background: Both chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea syndrome (OSAS) are common diseases. Previous studies suggested an increased prevalence of COPD among subjects with OSAS [1, 2]. More recent population surveys concluded contrary opinion [3].

Objectives: The study objective was to evaluate whether there is an epidemiological relationship between COPD and OSAS in a random population sample.

Materials and Methods: The study population, 356 males (53%) and 320 females, mean age 56.6 ± 8.2 years (range 41–72), was selected from a voting list for parliamentary election in Warsaw. The investigation included lung diseases and smoking history with polysomnography and spirometry.
Results: OSAS was diagnosed in 76 subjects (11.3%), 59 males (8.8%) and 17 females (2.5%), mean apnea/hypopnea index (AHI) was 25.3 ± 16.1, mean overnight SaO2 92.1 ± 3.3%, minimum SaO2 76.9 ± 9.4%, and SaO2 <90% = 18.9 ± 23.9% of total sleep time. COPD was diagnosed in 72 subjects (10.7%), 39 males and 33 females. Severity of airflow limitation was assessed according to European Respiratory Society (ERS) guidelines: mild in 70%, moderate in 22%, and severe in 8%. In 7 subjects (9.2% of OSAS population, 1% of total population) OSAS and COPD overlapped. Polysomnographic variables were compared between overlap (overlap syndrome, OS) and OSAS subjects. In the OS mean AHI was 19.0 versus 25.3 in OSAS (not significant), mean SaO2 89.6 versus 92.3% in OSAS (p < 0.005), and time spent in SaO2 <90% was 25.4 versus 18.2% in OSAS (p = 0.04).

Conclusions: COPD in subjects with OSAS was as frequent as in the general population. In the OS group mean arterial blood saturation was lower and time spent in desaturation was longer than in OSAS. The presented data suggest a more severe course of sleep-disordered breathing in subjects with coexisting COPD.

References

O 095
Insomnia Complaints and Lifestyle Factors in Women
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Aims: To investigate prevalence rates of insomnia complaints and their possible relationships with demographic variables and lifestyle factors in women.

Methods: Ten thousand randomly selected women from the general population of Uppsala municipality from 20 years of age and above were sent a postal questionnaire. Response rate was 71.6%. Insomnia complaints were defined as severe or very severe difficulties initiating sleep (DIS) or maintaining sleep (DMS).

Results: Of all women 9.0% had DIS, 15.1% had DMS, and 20.2% had either DIS or DMS. Women who were single, divorced or widows more often reported DIS than married or cohabitant women (12.1% vs. 7.5%, χ² = 39.8, p < 0.0001). The frequency distribution of DIS and DMS were significantly different between age groups (χ² = 29.6, p < 0.0001; χ² = 64.1, p < 0.0001). Lifestyle factors like physical inactivity and alcohol dependence were significantly (p < 0.0001) related to DIS and DMS. Overweight (BMI > 25) was significantly related to DMS (p < 0.0001) but only marginally to DIS (p < 0.05). Conversely, current smoking was significantly related to DIS (p < 0.0001), but not to DMS.

Conclusions: Unhealthy lifestyle factors like physical inactivity, alcohol dependence, overweight, and smoking were related to insomnia complaints in women. Therefore, such factors are worth noticing in the appropriate management of insomnia.

O 096
Subjective and Objective Measures of Sleepiness in a Large Sample of Commercial Truck Drivers
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Aims: We evaluated subjective sleepiness by Epworth Sleepiness Scale (ESS) in a large cohort of commercial truck drivers, and objective sleepiness with maintenance of wakefulness test (MWT) in a subsample of this cohort.

Methods: A detailed questionnaire, also including ESS, was sent to 2066 commercial drivers. 172 subjects were selected for sleep laboratory studies, including MWT.

Results: 1097 subjects returned the questionnaire (response rate 53.1%). Mean ESS was 7.5 (SD 4.1, range 0–24). In 47.1% of subjects ESS was at least 8, and in 30.2% it was at least 10 points. When we looked at individual questions in ESS we found out that only 2.1% reported that they had a moderate or high chance of dozing off when in a car while stopped for a few minutes in traffic.

Of 172 subjects evaluated in sleep laboratory 64 subjects had ESS at or above 10 points. Only 19 (26.7%) of these subjects had a mean sleep latency in MWT below 19.4 minutes, and in only 4 (6%) the mean MWT latency was below 8 minutes. When ESS was below 10 points, 1,9% of subjects showed a mean sleep latency below 8 minutes. In contrast, the mean MWT was 40 minutes in 20% of subjects when ESS was at or above 10 points.

Conclusions: About one third of commercial truck drivers in Finland report ESS at or above 10 points. Most of the questions in ESS, however, are not related to working situations. Indeed it was noted that only few subjects reported falling asleep while in traffic. A high ESS rating does not usually mean that a truck driver would not be able to sustain alertness in MWT. However, ESS points below 8 predict reasonably well that a subject is not sleepy.

O 097
Sleep Length and Mortality: A Population-Based 25-Year Follow-up Study
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1Finnish Institute of Occupational Health, Helsinki, Finland; 2The Finnish Twin Cohort, Dept. of Public Health, University of Helsinki, Helsinki, Finland; 3Skogby Sleep Clinic, Rimnekoti Foundation, Espoo, Finland; 4Dept. of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, Finland

Aims: An increased risk of mortality has been found in several studies in short and long sleepers, compared to average (7–8 h) sleepers. This relationship was studied in adult Finnish population.

Methods: In 1975 sleep length (5 hours or less, 6, 7, 8, 9, 10 hours or more) and sleep quality were asked in a questionnaire administered to the population-based Finnish Twin Cohort. The response rate was 89% (N=30,574 with no missing data on sleep variables, age 18 years or more). Covariates in the fully adjusted models (N=26,324) included hypnotic use, smoking, education, marital status, working status, social class, BMI, alcohol use, physical activity, and life satisfaction. Vital status and cause-of-death statistics up to 2001 were obtained from Statistics Finland. Cox proportional hazard models were used to obtain hazard statistics. The response rate was 89% (N=30,574 with no missing data on sleep variables, age 18 years or more). Covariates in the fully adjusted models (N=26,324) included hypnotic use, smoking, education, marital status, working status, social class, BMI, alcohol use, physical activity, and life satisfaction. Vital status and cause-of-death statistics up to 2001 were obtained from Statistics Finland. Cox proportional hazard models were used to obtain hazard ratios (HR) and their 95% confidence intervals (CI) for mortality by sleep length, using 7 hours as reference.

Results: During the 25-year follow-up (607,028 person years) 4341 subjects died. Those sleeping 7 or 8 hours had the lowest mortality. In age-sex adjusted HRs there was about a 20% increase in total mortality in short sleepers (6 h or less), and a 20–60% increase in long sleepers (9 h or more), and in fully adjusted models the increase was 10% and 10–20%, correspondingly.

Conclusions: Compared to average sleepers (7 or 8 h), there is about a 10% increase in mortality both in those sleeping less or more. This is not explained by covariates known to be associated with mortality.

O 098
Automatically detected EEG arousals in normal sleep: aging effects arousals in NREM and REM sleep differentially

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Introduction: EEG arousals in sleep are discussed as important markers of sleep disruption and/or as physiological indicators for the regulation of the sleep process. For the clinical application, both a reliable and valid automatic identification and normative data in healthy subjects are urgently needed to avoid the limitations of visual arousal identification (low inter-rater reliability, time-consuming and thus expensive).

Methods: Arousals were automatically detected in PSG recordings from 189 healthy controls (90 males, 99 females, 20–95 years). All data are taken from the second night after subjects’ adaptation to the experimental condition. In a first step, all recordings were classified automatically according to R&K by means of the Somnolyzer 24 × 7, which includes a sensitive automatic detection of sleep spindles2. In the second step, results were incorporated in an automatic identification of EEG arousals according to the ASDA (American Sleep Disorders Association) definitions. Basically, the EEG centroid frequency (frequency band: 4–40 Hz with 11.5–15 Hz excluded) at each local maxima was compared with a preceding 10-s sliding window to identify abrupt and transient (between 3 and 30 s) frequency changes.

Results: The arousal index (AI/h TST) was in young subjects (20–39 years) for males 17±6, for females 15±7; in middle aged subjects (40–59 years) for males 21±8, for females 14±6; and for older subjects (≥60 years) for males 26±12, for females 22±12. Thus, the AI was significantly higher in males than females (p<0.01) and increased independent of subjects’ sex by approximately 0.2 per year (r=0.38 and 0.33 for males and females, respectively; p<0.001). While a similar increase was observed for arousals in NREM sleep (specifically in S2 and in the first half of the night), the AI decreased in REM sleep (specifically in the last quarter of the night), both for males and females.

Discussion: The present normative values for automatically detected arousals in sleep, applied to baseline recordings in 189 healthy subjects, are in accordance with previously published data obtained with visual analysis in smaller sample sizes 3,4. Our data indicate the importance of reporting arousal indices separately for NREM and REM sleep.

O 099
Sleep Disorders Prevalence in a Representative Sample of Elderly Subjects of Santiago, Chile

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Introduction: In the last decades the Chilean population has gone through a rapid demographic and epidemiological transition process, which has determined a significant aging of the population and a progressive change of the major causes of death, with a significant increase of non-communicable chronic diseases (NCDs). Besides, there is now convincing evidence that sleep disorders (SDs) are indeed an independent risk factor for NCDs. Moreover,
studies on SDs prevalence, assessed in representative samples of elderly subjects, have not been carried out yet in South America. Therefore we recognize an urgent need for epidemiological studies on these issues.

Objectives: To describe the prevalence of SDs in a representative sample of elderly of Santiago, Chile, with respect to age, sex and socio-economic status (SES).

Subjects and Methods: This is a cross-sectional cohort study, carried out on a sample of 1301 elderly subjects (855 females and 446 men, age range: 60–99 years) selected with a probabilistic three step-procedure among the elderly population of Santiago de Chile, where more than 35% of the national population lives. All subjects of the obtained representative sample, were asked to complete a questionnaire on SDs. Statistical differences for age, sex and SES were assessed applying a chi² test.

Results: Among the 23.5% of subjects who stated to have SDs (26.4% of women and 18.1% of men, p < 0.004) only 37.0% reported to have referred to a clinician (41.7% of women and 25% of men, p < 0.004). 20.5% of subjects took drugs to sleep (25.0% of women and 12.1% of men, p < 0.01), and this percentage increased with age (p < 0.001). 62.7% of men referred to snore and 24.7% of them had obstructive sleep apnea, in women these percentages were 58.4% and 16.2% respectively; both these two SDs significantly decreased with age (p < 0.002 and < 0.006, respectively). 27.6% of subjects reported involuntary motor activity during sleep (25.4% of women and 31.7% of men, p < 0.05) and this percentage decreased with age (p < 0.05). No significant difference for SES was observed for any of the SDs described but insomnia. Namely 30.0% of the richer elderly reported to have problems in maintaining sleep compared to only 10.6% of the poorer (p < 0.01); while 29.5% of richer elderly reported disorder in initiating sleep compared to 49.1% of the poors (p = 0.002).

Conclusion: Our results show a very high prevalence of SDs among the elderly of Santiago de Chile, with important differences for age, sex and even for SES. Given the association between SDs and NCDS, we suggest that further studies should investigate to which extent SDs impact on morbidity and mortality in this age group.

O 100
The self-assessment scale for sleep and awakening quality (SSA)-Normative data and polysomnographic correlates

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Introduction: While polysomnography is the gold standard for evaluating objective parameters of sleep, several tools for measuring subjectively experienced quality of sleep have been described in the literature. The self-rating questionnaire for sleep and awakening quality (SSA, Saletu 1987) is an easily practicable test, which can be completed in approximately two minutes. It was validated and normative data were collected in a large database of healthy volunteers during the European project SIESTA.

Methods: The SSA consists of 20 items and yields three sub-scores-for sleep quality (SSA-1), awakening quality (SSA-2) and somatic complaints (SSA-3)-as well as a total score. 195 healthy controls aged between 20 and 95 years (divided into 7 age groups) completed the self-rating questionnaire every morning for two weeks. On days 7 and 8 of the reported period the subjects spent two consecutive nights in the sleep laboratory. To assess the correspondence between SSA and polysomnographic measurements, change values between the 2nd and the 1st night were determined for objective R&K values (as obtained by means of the Somnolyzer 24x7) as well as for subjective SSA values. Subsequently, these changes were subjected to correlation analyses.

Results: In both objective and subjective sleep quality a first-night effect was observed independent of age. In contrast to objective R&K values, subjective sleep quality of healthy controls did not change with increasing age and there was no appreciable difference between male and female subjects. Subjective sleep quality was found to be significantly correlated (p < 0.001) with sleep efficiency (r = .461), wake within total sleep time (r = −.381), total sleep time (r = .340), and the number of awakenings per hour of sleep (r = −.311). With respect to sleep architecture, subjective sleep quality was correlated with the time spent in sleep stage 2 (r = .261) as well as in stage REM (r = .286), but not with the percentage of S2 or REM. Partial correlations-controlled for the effect of total sleep time-revealed that the time spent in S2 and REM was not directly related to subjective sleep quality.

Discussion: The results indicate that the SSA is a sensitive measure of even small intra-individual changes of sleep quality (such as the first-night effect). Subjectively experienced sleep quality in healthy controls seems to be primarily influenced by sleep efficiency and thus by the amount of wakefulness during the night. This relationship was not affected by age or gender.
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Aims: Over 65 million Americans experience sleep related difficulties. Sleep disorders (SD) can affect cardiovascular health, cognitive functioning, and lead to behavioral problems. The presence of SDs is not specific to age, yet the presentation of these disturbances and the consequences on an individual’s health changes as a result of the natural aging process.

Assessment of sleep problems is inadequate across all age ranges. Ignorance regarding sleep is ubiquitous spanning all age groups, and even more so when considering information regarding distinguishable characteristics in epidemiology, symptoms, and psychological effects of sleep problems across the life-span. Further complicating matters, there is debate on how to best classify people by age. Many of the current classifications used are too broad and may not be sensitive to changes over time.

Methods: Accordingly, we investigated SDs and related symptoms by defining three separate methods of age categorization: (1) participants were classified as child/youth (16 or under), adult (17–64), or geriatric (65+); (2) Five generation classifications (USA 2000 census); and (3) classified participants into 11 different age cohort groups based on developmental, social, psychological, and environmental influences. We assembled an interdisciplinary team and constructed a 111-item questionnaire to assess sleep habits, sleep observations, past medical and psychological history, prior treatment approaches for SDs, social information, and medications. We used the questionnaires in conjunction with NP studies, multiple sleep latency tests (MSLT), the Epworth Sleepiness Scale (ESS), and medical chart reviews of people referred to our institution for evaluation of SDs.

Results: We compared age appropriate data for 450 people who were referred for evaluation of sleep problems based on age group, generation, and age cohort. Examples of significant differences across all three group classifications include: the number of hours spent asleep each night, waking with a choking sensation, waking rested, sleepiness affecting work/school and social activities, accidents related to sleepiness, having bizarre dreams, feelings of stress and irritability, consumption of alcohol and caffeine, and the amount of time spent in stages 1, 3, and 4 of sleep revealed in NP. Other significant differences between ages were found only when using age cohort or generation classifications for analysis and included such findings as differences relating to falling asleep resting after lunch, stopping breathing during sleep, and grinding teeth during sleep.

Conclusions: The differences observed when using more specific methods of grouping participants by age indicates that studies specific to changes in sleep habits and problems across the life-span deserves merit. Indeed, given the numerous negative health and social impacts of SDs, it is important to understand sleep across the ages.

O 102
Siesta and Sleep Disorders at Night: Prevalences and Associations with Cardiovascular Diseases and Risk Factors

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Introduction: The association between siesta (afternoon nap) and health outcomes remains controversial. Kalandidi et al. found a protective effect of regular siesta in a Greek case-control study (Kalandidi et al., 1992). In contrast, Campos et al. found in a case-control study in Costa Rica that regular siesta is associated with an increased risk of myocardial infarction (Campos et al., 2000). Here we report population-based prevalence estimates of siesta and sleep disorders at night and show how they are related to cardiovascular and other diseases.

Material and Methods: The Heinz Nixdorf Recall Study is an ongoing population-based prospective cohort study of the comparative predictive value of modern risk stratification techniques for coronary events (Schmermund et al., 2002). Overall, 4,814 subjects aged 45–75 years were included in the study. The baseline examination included a questionnaire-based cardiovascular risk assessment, anthropometric measurements, blood pressure measurements among others. The questionnaire included several questions on sleep disorders at night (difficulties falling asleep and maintaining the sleep, early morning awakening) and siesta (frequency and duration). About 327 out of 4814 subjects had a history of coronary artery disease (CAD). We calculated sex- and age-specific prevalence estimates of siesta and sleep disorders at night. We used log-linear regression models and calculated age- and sex-adjusted prevalence ratios (PR) and 95% confidence intervals (95%CI) using SAS (PROC GENMOD).

Results: Men have a higher prevalence of regular siesta than women in all age groups. All forms of sleep disorders at night were more often reported among women than men. With the exception of early morning awakening, all sleep disorders at night increased by age. We found increased prevalence ratios of siesta after adjusting for age and sex among subjects with: coronary artery disease (CAD) (PR = 1.37; 95%CI 1.11–1.69) and peripheral arterial disease (PR = 1.22; 95%CI 0.89–1.69). The prevalence of regular siesta of at least one hour was considerably higher among
subjects with CAD (PR = 1.50; 95% CI 1.12–2.02). Subjects with CAD more often reported difficulties maintaining the sleep (PR = 1.25; 95% CI 1.11–1.41) and less often difficulties falling asleep (PR = 0.93, 95% CI 0.89–0.98) and less often early morning awakening (PR = 0.94, 95% CI 0.90–0.98) compared to subjects without CAD. Subjects with regular siesta more often reported difficulties falling asleep (PR = 1.45 (95% CI 1.19–1.76), and early morning awakening (PR = 1.33 (95% CI: 1.09–1.61)) also after adjustment for age, sex, and CAD.

Discussion: Subjects with known CAD have higher prevalences of siesta and difficulties maintaining sleep at night than subjects without CAD. The association between siesta and sleep disorders at night as well as comorbidity makes the interpretation of the current literature on siesta and risk of myocardial infarction difficult.

O 103
Napping is Associated with Increased Risk of Non-Spine Fractures in Older Women

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Aims: We previously found that older women who self-report napping every day are at increased risk of falls and fractures. Therefore, using actigraphy we investigated whether objective measures of napping are associated with risk of subsequent non-spine fracture in older women. We further assessed if this relationship is independent of other potential covariates such as depression, comorbidities, fall history and bone mineral density.

Methods: We studied 2939 older community-dwelling women (mean age 83yrs) who participated in an eighth round of clinic visits in the prospective Study of Osteoporotic Fractures, from 2002–2003. Objective measures of sleep and napping from actigraphy were gathered using the Sleepwatch-O from Ambulatory Monitoring, Inc. Data gathered in the proportional integration mode was used for this analysis. Participants were contacted every 3 months by questionnaire or phone, to prospectively assess the occurrence of incident non-spine fractures. All reported fractures were confirmed by centralized review of radiology reports. Cox proportional hazards models were used to adjust for age, depression, history of falls, bone mineral density, comorbidities, and other covariates.

Results: Of the 2939 women with data on napping obtained by actigraphy, 202 women suffered a subsequent non-spine fracture during approximately 2.5 years of follow-up. After adjusting for covariates, women who napped at least 30 minutes per day had a 60% increase in risk of non-spine fracture (relative hazard = 1.6; 95% confidence interval 1.1 to 2.3) compared to women who napped fewer than 30 minutes per day. There was no evidence of a dose-response effect with greater duration of napping (table). Indices of night-time sleep (e.g. total sleep time and sleep fragmentation) were unrelated to risk of fracture.

Conclusions: Daytime napping is associated with increased risk of non-spine fractures in older women. Napping may be a surrogate for inactivity, or may reflect an underlying sleep disorder such as sleep disordered breathing.

O 104
Age dependency of sleep parameters

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Aims: Changes of sleep structure with age have different subjective and objective aspects and it is a significant problem for many elderly adults and has multifactorial origin.

Methods: The SIESTA project included 195 healthy subjects (102 women, 93 men) of all age groups between 20 to 95 years (mean age: 51.5 ± 19.4 years); subjective (PSQI, sleep diary) and objective (sleep polygraphy) measurements of sleep were performed. The Pittsburgh Sleep Quality Index (PSQI) evaluates habitual sleep efficiency, sleep latency, sleep duration sleep habits and subjective ratings of sleep quality retrospectively. Sleep logs were used to document daily habitual sleep time and efficiency. Polysomnographic sleep recordings were analysed visually (Rechtschaffen and Kales (R&K)) and automatically (SIESTA sleep analyser). Sleep spindles were automatically identified. Subsequently, eighteen characteristics of the automatically identified spindle epochs were computed and summarized for NREM stage 2 sleep. The effect of age on the obtained measures was investigated by means of Spearman rank correlation.

Results: Subjective variables: PSQI-questionnaire for all subjects revealed a sleep period time about 451 min (±
Objective variables: Slow wave sleep (stage 3 and 4 according to R&K) decreased with age, whereas the automatic analysis regarding only frequency bands (without amplitude information) showed nearly no relevant changes with age. Sleep spindles: Fifteen out of 18 investigated variables were significantly reduced by age: the absolute number, density, mean duration, total and relative spindle time, maximal and mean amplitude as well as mean frequency. In the youngest age group (30–39 years), gender differences were exhibited mainly in higher amplitude measures in females. In the oldest age group (> 60 years), men showed significantly fewer spindles, lower spindle densities and lower amplitudes, as compared to women.

Discussion: Results demonstrate that subjective ratings of sleep are significantly influenced by the kind of questionnaires. Retrospective estimates of sleep efficiency, sleep latency and sleep duration as represented by the PSQI, provide a more “idealistic” view of one’s habitual sleep than actual ones represented by sleep diaries. The decrease of slow wave sleep of elderly is dependent on the actual ones represented by sleep diaries. The decrease of sleep efficiency of 91.84% (±7.5%) the same variables calculated from the sleep diaries, showed significant differences (p=0.01): a prolonged sleep latency (18.63 min; ±13 min), reduced sleep efficiency (86.81%; ±7.16%) as well as a shorter sleep period time (438 min; ±51.15 min), showing only significant differences in females. Results did not show any age-related interactions.

Instrumentation/Methodology

O 105 Concurrent validity of the Somnolyzer 24x7 based on results from a neuropsychopharmacological sleep laboratory study

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When developing a new quantification tool quality measures must be performed. Concurrent validity should be assessed in addition to reliability and face validity. To determine concurrent validity of the Somnolyzer 24x7 (TM) [1], we utilised polysomnographic recordings obtained from 11 healthy young volunteers of both sexes participating in a double-blind, double-dummy, placebo-controlled, repeated-dose, 4-period, cross-over study. All participants had received a morning dose of paroxetine 20 mg, alprazolam 1 mg, paroxetine 20 mg + alprazolam 1 mg, or placebo. Acute effects (night 1) and steady-state effects (night 15) were evaluated. All 30-second epochs were scored twice on the basis of Rechtschaffen & Kales criteria: (i) visually, by two blinded independent experts with a third scorer to resolve any discrepancies, and (ii) automatically, by a computer-assisted sleep analysis system-Somnolyzer 24x7-. Variables evaluating sleep initiation and maintenance sleep architecture and non-REM-REM periods were subsequently computed and experimental hypotheses were statistically tested based on the two independent sets of data. Although systematic differences between mean visually- and automatically-derived variables were observed, above all in sleep architecture (visually: more time on S2 and REM and less time on S1 and SWS), statistical conclusions were essentially the same in both sets of data. The same research answers were achieved utilising either human or computer resources, thus showing the feasibility of computer-assisted sleep analysis systems, particularly when dealing with neuropsychopharmacological questions.


O 106 The relationship between Rechtschaffen and Kales derived measures of sleep based on human experts or Somnolyzer 24x7 evaluations

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**Introduction:** Conventionally, polysomnographic recordings are classified according to the rules published in 1968 by Rechtschaffen and Kales. For statistical analysis, measures such as sleep latency, sleep efficiency or time and percentage of the different sleep stages are quantified on the basis of the hypnogram obtained. The present paper compares target variables derived from hypnograms obtained either by human expert scoring or by means of a newly developed automatic classifier.

**Methods:** The Somnolyzer 24 × 7™ adheres to the decision rules for visual scoring as closely as possible and includes a structured quality control procedure by a human expert. The final system consists of a raw data quality check, a feature extraction algorithm (density and intensity of sleep/wake-related patterns such as sleep spindles, delta waves, slow and rapid eye movements), a feature matrix plausibility check, a classifier designed as an expert system, a rule-based smoothing procedure for the start and the end of stages REM and 2, and finally a statistical comparison to age- and sex-matched normal healthy controls (Siesta Spot Report™). The presented results are based on the validation data of the Siesta polysomnographic database (286 recordings in both normal healthy subjects aged 20 to 95 years and patients suffering from organic or nonorganic sleep disorders).

**Results:** Validation demonstrated an overall epoch-by-epoch agreement of 80% (Cohen’s Kappa: 0.72) between the Somnolyzer 24 × 7 and the human expert scoring, as compared with an inter-rater reliability of 77% (Cohen’s Kappa: 0.68) between two human experts. Two Somnolyzer 24 × 7 analyses (including a structured quality control by two human experts) revealed an inter-rater reliability close to 1 (Cohen’s Kappa: 0.991). Moreover, correlation analysis in R&K derived target variables showed a similar-in 36 out of 38 variables even higher-correlation between the Somnolyzer 24 × 7 and expert evaluations as compared to the concordance between two human experts.

**Discussion:** Thus, the validation study proved the high reliability and validity of the Somnolyzer 24 × 7 on both the epoch-by-epoch and the target variable level. These results demonstrate the applicability of the Somnolyzer 24 × 7 evaluation in clinical routine and sleep studies.

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**O 107**

**Fractal Method for Sleep Staging and for Wakefulness/Sleep Monitoring Based on EEG-Signal Analysis**

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**O 108**

**Continuous and parametric description of sleep EEG**

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**Aims:** Improvement of sleep/wakefulness monitoring requires simple and quick assessment of vigilance through analysis of biosignals. Also diagnostics of sleep disorders will benefit from quick assessment of sleep dynamics through computerized construction of hypnograms.

**Methods:** Nonlinear time series analysis, in particular fractal and symbolic methods of analysis in time domain, are well suited to achieve these goals.

**Results:** We have demonstrated that despite of great individual differences and the lack of any ‘golden standards’ Higuchi’s fractal dimension of EEG-signal diminishes during transition from wakefulness to stage 1 sleep and further to stages 2, 3, 4, and then increases again during REM. The sleep stager we built up based on fractal dimension of EEG-signal constructs the hypnogram from a whole-night EEG-data in a very short time of 2–3 min. Since there are big differences between specialists in sleep scoring while using RK scale our stager may be ‘trained’ on the scores made by the specialist who is going to use the stager and then ‘fine tuned’ for better agreement. Even simpler may be using of the same method for monitoring vigilance e.g. of truck drivers. The system may be ‘fine tuned’ by the driver for personal use, activating a warning signal ‘Beware, you may be falling asleep!’.

**Conclusions:** Biosignal analysis using methods borrowed from Nonlinear Dynamics and Fractal Geometry may be very useful and efficient in sleep research and its everyday applications.
e.g. sleep spindles and slow waves, based directly upon the classical definition of these structures.

**Results:** We present successful parameterization and automatic detection of delta waves and sleep spindles and also possibility of detection of different events like arousals in all-night EEG sleep data. Apart from the new continuous descriptors of the overnight sleep process, within the same framework are proposed detection of deep sleep stages (based directly upon the classical R&K criteria) with concordance on the level of the inter-expert agreement.

**Conclusions:** Adaptive time-frequency parameterization provides a bridge between the advanced signal processing and the traditional, visual analysis. Proposed paradigm provides description of the major features of sleep EEG in a way compatible with traditional, visual analysis.

### O 109
**A new data acquisition system for monitoring circadian variations of activity and ECG: Technical aspects**

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**Aims:** Sleep disturbances are often accompanying somatic, neurologic and psychiatric disorders. But today, they are usually not evaluated quantitatively/objectively, although they may provide useful information about the course of the primary disease, as for example in depressive patients. For this reason, a dedicated data acquisition system has been developed that can be integrated into the clothing of the patient (e.g. into underpants or pyjama) and that allows long-term monitoring of sleep, but also of daytime activity.

**Methods:** The data acquisition system consists of a textile and an electronic module. The textile can be attached to the waistband of standard underpants by means of snap fasteners. It contains 3 rubber electrodes for 1-lead ECG measurements, a temperature sensor and a pocket for taking up the electronic module. The electronic module consists of several circuit boards which are mounted on a flexible metal rack. It contains the following units:

- analog ECG preprocessing
- 2D accelerometer (for measuring the patient’s activity)
- digital unit (microprocessor and 128 MB memory)
- accumulators (energy lasts for 5 days of measurements)
- communication unit (Bluetooth link to PC)

The electronics are coated with a foam material in order to protect the electronic components and to enhance the comfort for the patient. So far, the system has been tested in a clinical setting on 12 patients for periods of 4–12 weeks respectively.

**Results:** As for hardware reliability and robustness the following failures have occurred during the measurements: One electronic module broke mechanically, another broke down due to electrical problems. As for the textile, in one piece two electrodes had to be replaced, one because of a broken cable. As for signal quality, it has been observed that the quality of the ECG signal highly depends on the physical activity of the patient. The more active the patient is, the more motion artefacts are found on the ECG signal. But during sleep, the ECG quality is in general sufficient for the designated calculations of heart rate and heart rate variability (HRV). The time in bed (TIB) as well as the movement time (MT) are clearly identifiable from the accelerometer signal. This will be presented in detail.

**Conclusion:** The reliability and the robustness of the data acquisition system seem to be acceptable for a clinical setting. The integration of the data acquisition system is also perceived as advantageous because it enables discreet and at the same time comfortable measurements. The signal quality of the ECG and the activity measurements meet the requirements. By placing the activity sensor at the patient’s trunk, the measurements map the patient’s overall activity very reliably. The body temperature signal still seems to be subject to too many external influences. This will be subject to further investigations.

### O 110
**The temporal distribution of sawtooth waves at the onset of REM sleep**

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**Introduction:** Sawtooth waves (STW) are a typical EEG pattern of REM sleep in the frequency range 2 to 6 cycles per second with a characteristic appearance (slow negative upward phase, followed by a steep positive deflection). The source and function of STW are unknown. STW occur intermittently, frequently in association with REM bursts. STW can also occur in stage 2 sleep just before REM sleep. We studied the temporal distribution of STW before and after the onset of REM sleep.

**Methods:** Polysomnographic (PSG) recordings of 20 subjects (12 w, 8 m, mean age 51.0 years, SD 18.5 years) were analysed. The sample was randomly drawn from our clinical data bank. PSG recordings contained 4 EEG channels (F1-A1, C3-A2, C4-A1, and O2-A2), 2 EOG, 4 EMG, 1 ECG and 3 respiratory channels. In a first step, the last 20 epochs immediately preceding REM and the first twenty epochs into REM sleep were extracted and stored. In a second step, all 30s epochs were subject-wise rearranged
in random order to prevent scoring bias. Epochs were scored visually by one of us (HS). For each epoch the presence or absence of STW was scored. In a final step the scoring tables were rearranged into the correct temporal order for further analysis.

Results: STW increased steeply in the last four minutes before REM sleep onset and reached a pronounced peak in the first minute of REM sleep. Thereafter, STW decreased again to reach a low level after four minutes into REM sleep. The SWT density was lowest (.027) at baseline (10 to 4 minutes before REM sleep onset). It increased to a value of .269 at the time of the peak and approached a plateau of about .060 after four minutes of REM sleep.

Discussion: STW displays a specific temporal pattern with an early peak in REM sleep, followed by a rapid decline. It belongs to those physiological events which start shortly before REM sleep and may be associated with the initiation of REM sleep. Although STW may occur near bursts of eye movements in REM sleep, the observed temporal distribution suggests a remarkable degree of independence of these two phasic events.

O 111
Multicenter Validation Study on the Sleep Stage Scoring Variability of the Algorithm ARTISANA Compared to Human Experts

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Introduction: ARTISANA is an algorithm for recognizing sleep stages according to Rechtschaffen and Kales, which contains adaptive inference and models the different decision steps of visual scoring. It was shown before that agreement rates with a single human scorer are not very meaningful as they are significantly influenced by the selection of recordings. Conclusions about the scoring quality can only be drawn if agreement rates of human scorers are used as a reference.

Methods: In this multicenter validation study, 50 recordings from patients with sleep disorders (age: 54±11 years, 13 OSA, 13 Insomnia, 14 normal sleep profile, 10 others e.g. RLS or CSA) were scored by ARTISANA and 6 experienced European sleep centres: Barcelona, Berlin, Grenoble, Gothenburg, Palermo and Turku.

For each scorer, the majority decision of the remaining 5 scorers for each epoch was used as a reference. The ARTISANA scorings were compared to the same reference to assess agreement (Cohens kappa and percentage). Statistical equivalence was tested by Passing-Bablock-Regression and differences were assessed by t-test.

Results: The agreement rates with the corresponding reference were shown to be equivalent for 4 sleep centres compared to ARTISANA. In one case, the agreement with the reference of the sleep centre was higher than the one of the algorithm and for one sleep centre it was lower.

Conclusion: The algorithm performed with a quality similar to the one of 6 experienced human scorers. It is objective, efficient, fully reproducible and provides a high quality of results. Thus, it has the potential to standardize and quantitatively compare evaluations to a degree never reached before in clinical practice and research for the diagnosis of OSA and other sleep disorders.

O 112
A portable monitoring device for obstructive sleep apnea diagnosis- a new validation standard using in a population based cohort?

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Study Objective: To assess the accuracy of a portable monitoring device based on peripheral arterial tonometry to diagnose obstructive sleep apnea (OSA). To propose a new

<table>
<thead>
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<th>Reference</th>
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<th>Median % agreement scorer</th>
<th>Median Kappa ARTISANA</th>
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standard for limited-channel device validation using synchronized polysomnography (PSG) home recordings and a population-based cohort.

**Design:** Single-night, unattended PSG and Watch_PAT 100 (WP_100). Setting: Home environment and primary health care centre.

**Participants:** 98 subjects (55 males, age 60±7 yrs, body mass index 28±4 kg/m2, 21 hypertensives and 2 with diabetes) randomly selected from the Skaraborg Hypertension and Diabetes Project. Interventions: N/A.

**Measurements and Results:** The WP_100 records peripheral arterial tone, heart rate, arterial oxygen saturation and actigraphic signal for automatic analysis of respiratory disturbance index (RDI), apnea hypopnea index (AHI), oxygen desaturation index (ODI) and sleep-wake state. The accuracy of WP_100 in RDI, AHI, ODI and sleep-wake detection was assessed by comparison with data from simultaneous PSG recordings. The mean PSG AHI in this population was 25.5±22.9 events per hour. The WP_100 RDI, AHI, ODI correlated closely (0.88, 0.90 and 0.92, P<0.0001, respectively) with the corresponding indices obtained by PSG. The AUC’s for the ROC curves for WP_100 AHI and RDI were 0.93 and 0.90 for the PSG AHI and RDI thresholds 10 and 20 (P<0.0001, respectively). The agreement of the sleep-wake assessment based on 30 seconds bins between the two systems was 82±7%.

**Conclusions:** The WP_100 was reasonably accurate for unattended home diagnosis of OSA in a population sample not pre-selected for OSA symptoms. The current design including simultaneous home PSG recordings in population-based cohorts is proposed as a reasonable validation standard for assessment of simplified recording tools for OSA diagnosis.

**Physiology/Endocrinology**

**O 113**

**Estrogenic hormonal function, age and development of OSAS in women**

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**Objectives:** To assess influence of female hormonal function on breathing during sleep.

**Materials and Methods:** Random population sample of 320 women, originally involved in Polish branch of MONICA II study, mean age 56.2±8 years (range 41–72), had history of sleep disordered breathing (SDB) taken, polysomnography recorded and daytime sleepiness measured using Epworth Sleepiness Scale (ESS). Hormonal status was assessed using self-reported questionnaire. 107 women menstruated either spontaneously or using hormonal replacement therapy (HRT). 213 of them did not menstruate due to menopause (171), hysterectomy (34) or from unknown reasons. 20 of non-menstruating ones used HRT. In a whole sample 40% of women were concluded as having estrogenic activity. One-way ANOVA was used to test differences between estrogenic (E) and non-estrogenic (non-E) subjects. Than analysis of covariance (ANCOVA) was used to adjust data for age and BMI. As covariates mean values (age, BMI) of non-E group were used.

**Results:** Women having estrogenic activity were younger (49.5 vs 61.0 years, p<0.001), had lower apnea hypopnea index (AHI, 2.2 vs 5.8 per hour, p<0.001), higher mean SaO2 (94.1 vs 93.1%, p<0.001) and minimal SaO2 (83.9 vs 79.9%, p<0.001), lower oxygen desaturation index (ODI, 6.7 vs 11.7 per hour, p<0.01) and spent minority of time with saturation <90% (T90, 5.0 vs 11.7%, p<0.005) compared to women without estrogenic activity, respectively. Among 16 subjects diagnosed with OSAS, only one (6%) originated from estrogenic group (1 vs 15, p<0.01). After adjustment for age and BMI no longer differences between E and non-E groups remained statistically significant.

**Conclusions:** ANOVA showed that OSAS was more frequent and SDB were more severe in women in non-E group. However, after adjustment for age and BMI no significant differences in polysomnographic variables as well as in sleepiness were shown between both studied groups.

**O 114**

**EEG Power Spectral Analysis of the Cyclic Alternating Pattern in Normal Subjects**

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Sixteen normal subjects underwent 1 polysomnographic night recording, which included: EEG, EOG, chin EMG, EMG of the tibialis anterior muscles, and ECG. Sleep stages were scored and all CAP A phases detected and classified into 3 subtypes (A1, A2, and A3). The channel used for the detection of CAP A phases was subdivided into 2-second mini-epochs, only those from sleep stage 2 and sleep stages 3 or 4 (SWS) were considered. For each mini-epoch, the corresponding CAP or NCAP condition was determined. Power spectra were calculated for frequencies between 0.5 and 25 Hz with a frequency step of 0.5 Hz. Average spectra were obtained for each CAP condition, separately in sleep
O 115
Reversals in the direction of information flow between the cerebral hemispheres while falling asleep and during awakening from NREM sleep in humans: an EEG study of hemispherical dominance in sleep

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Despite overwhelming evidence for lateralisation of many cerebral functions in wakefulness, only minor insights have been gathered concerning functional asymmetry between the two hemispheres in sleep. However, since movements in both NREM and REM sleep occur preferentially in the non-dominant hand (Jovanovic, 1971; Lauerma et al., 1992) the hypothesis has been advocated that functional asymmetry might also be present in sleep, but that cerebral dominance may be inverted as compared to that in wakefulness. Further, studies using frequency analysis techniques in healthy subjects and acallosal patients have revealed that interhemispheric functional connectivity is present in all sleep stages (Montplaisir et al., 1990), though power and degree of coherence differ between homologous cerebral sites (Nielsen et al., 1990). Here we address the question of interhemispheric functional asymmetry in sleep in healthy subjects using the directed transfer function (DTF) to analyse surface EEG. The DTF investigates the direction of flow of coherent activity, a surrogate maker of information exchange, between regions (Kaminski & Blinowska, 1991). As such, the net flow of coherent activity (information) between two recording sites can be assessed by subtracting the DTF flow from one direction from that in the opposite direction. Additionally, DTFs can be plotted as time-evolving spectra (Sharott et al., 2005), so that the relationship between the directions of information flow between sites can be correlated with events, such as awakening. We can show in two healthy subjects that net DTF flow is reversed in appropriate frequency bands while falling asleep and during awakening. In the first, left-handed subject, there was a net DTF flow from right to left cortical sites in the a-range before falling asleep. In the process of falling asleep this net right to left flow was gradually replaced by a net left to right flow of information in the d-frequency range during NREM sleep. With spontaneous awakening from NREM sleep the net information flow in the right to left direction was re-established in the a-range. Similar changes were identified in the second, right-handed, subject, both while falling asleep and during awakening, with the exception that the net directions of information flow were inverted as compared to the left-handed subject. These results support the hypothesis of inverted cerebral dominance during sleep. If confirmed in a larger sample then they have significant implications for the study of cognitive function and neural plasticity in sleep.

O 116
A Neural Network Based Analysis of the Electroencephalogram in Sleep Stage 2 Concerning the Elicitability of Evoked K-Complexes

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Aims: K complexes (KC) are beside spindles the most prominent signs of sleep in stage 2. Until now their significance is not fully understood and deviations from their normative features observed in polysomnography have still gained no clinical importance. KC seem to be elements of an arousal reaction mobilizing simultaneously also sleep protective processes. We asked if the elicitability of evoked KC is depending on the cortical state which should be reflected by EEG characteristics in pre-stimulus-intervals (PSI). A precursory investigation of 16 subjects showed no differences of EEG power spectral densities in PSI. The aim of this work was to verify these results using more subjects and by an improved Neural Network methodology.

Methods: 24 adults (13 women, 11 men; mean age: 25.3 years, SD 7.2, range 18–47) spent a single night in the laboratory. Pairs of tone clicks with an inter-stimulus-interval of 3 sec were presented every 20 to 30 sec randomly. Inside visually scored stage 2 four elicitability responses (00, 10, 01, 11) were classified regarding occurrence (1) or non-occurrence (0) of KC on first and second stimuli respectively. EEG of PSI was analyzed utilizing four different methods of spectral estimation and two different wavelet filter banks. Obtained parameters were put into a discriminant analysis utilizing five different types of Artificial Neural Networks.

Results: All in all 7,412 responses were analyzed. Elicitabilities of KC responses vary largely: (59 ± 18) % for 00, (9 ± 3) % for 01, (23 ± 10) % for 10 and (9 ± 9) % for 11. Elicitability of KC on the second stimulus [(17 ± 11) %] is lower than on the first [(32 ± 17) %]. All different methods utilized for EEG analysis in PSI resulted same: there are no differences in spectral and wavelet parameters of the EEG in PSI when KC are occurring or not.

Conclusions: Elicitability of KC on the second stimulus is halved compared to the first stimulus; it is lower, when a KC is evoked by the first stimulus. But generally, elicitability is independent of EEG running before the stimulus. Cortical states reflected by characteristically EEG alterations are not verifiable. Decisions on eliciting KC seem to be generated in subcortical, probably thalamic, structures. Drastic reductions or the absence of spontaneous KC might give hints on malfunctions of subcortical structures. Further neurological-polysomnographic investigations might serve for supporting contributions.

O 117

Hypocretin-1 levels in a 18-year-old boy with Kleine-Levin Syndrome

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Introduction: Hypocretin-1 and -2 play a significant role in the regulation of both feeding and sleep-wake cycles1. Hypocretin levels are known to be drastically decreased or undetectable in narcoleptic patients2. Kleine-Levin Syndrome (KLS), which is characterised by recurrent acute episodes of hypersomnia, abnormal feeding behaviour, and inconstant and transient psychiatric manifestations3, might represent a model disorder for hypocretin system dysfunction.

Evidence on CSF hypocretin-1 levels in patients with Kleine-Levin Syndrome during acute phase is very limited. Only two case reports specifically addressed this issue. In the first report of a 20 year-old male, results showed a moderate decrease in the CSF hypocretin-1 levels when comparing measures during acute and asymptomatic phase (221 pg/ml vs 111 pg/ml, respectively)4. In the second case of a 15 year-old male, CSF hypocretin-1 levels during acute phase were reported as normal, but the measure was not specified by the authors5.

Case report: An 18-year-old boy, diagnosed with KLS at the age of thirteen years, was seen at the outpatient clinic of the Child Psychopathology Unit four days after the onset of the fourth episode of recurrent hypersomnia. The episode started on the week-end after moderate alcohol intake and sleep deprivation. The boy presented with extreme fatigue, clinophilia, sleepiness, abnormal feeding behavior (taste alteration with hyporexia and preference for particular foods), irritability, aggressiveness, and moderate behavioural disinhibition. No psychotic symptom was found. The patient was apyretic and had no clinical sign of infectious episodes. A decrease in the severity of the symptoms was noted the day the patient came to the clinic. Lumbar puncture, as well as a 24 hours polysomnographic recording, were performed five days after the onset of the episode.

The laboratory findings will be discussed and detailed in relation to the clinical symptomatology (i.e. ending of an acute episode) as well as to the previous published data.

References

O 118

Recruitment patterns of spinal motoneurons in human sleep as assessed by f-wave recordings

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Aims: This study examines recruitment patterns of spinal motoneurons in human sleep. Though reduced excitability of spinal motoneurons has previously been shown in sleep it still remains open whether inhibition affects the entire spinal motoneuron pool in the same way and to the same extent in NREM and REM sleep. To address these questions we assessed F-tachoeidispersion alongside conventional f-wave-parameters (F-persistence, F-amplitudes) in 17 healthy subjects in NREM2, NREM3/4, REM and wakefulness.

Methods: Stimuli were delivered on the ulnar nerve at wrist level with a stimulus intensity of 1.2 times of the sleep-stage specific maximal M-response at a frequency of 0.2 Hz. Compound muscle action potentials were recorded from the 1DI muscle. For analysis repeated sets of at least 128 stimuli were stored to obtain 15 artefact-free F-waves. F-tachoeidispersion was calculated based on F-conduction-velocities using the modified Kimura-formula (Chroni and Panayiotopoulos, 1993).

Results: F-persistence (ratio sleep-stage/wakefulness; NREM 2: 0.46 ± 0.11; NREM3/4: 0.36 ± 0.09; REM: 0.14 ± 0.05) confirmed decreased spinal excitability in all sleep-stages, most markedly in REM as did F-amplitudes (ratio sleep-stage/wakefulness; NREM2: 0.45 ± 0.08; NREM3/4: 0.38 ± 0.06; REM: 0.35 ± 0.15). The range of F-tachoeidispersion (ratio sleep-stage/wakefulness; NREM2: 0.82; NREM3/4: 0.82; REM: 0.64) was reduced in all sleep stages with a shift (difference between medians of sleep-stages and wakefulness; NREM 2: -1.84m/s; NREM 3/4: -2.31; REM: -0.05) towards lower conduction-velocities in NREM.

Conclusions: Our study shows sleep-stage specific reduced excitability of spinal motoneurons. Variations in shifts of F-tachoeidispersion suggest that supraspinal inhibitory mechanisms might act differently on fast-conducting spinal motoneurons in NREM and REM

O 119

Functional connectivity in the human motor system across the sleep-wake cycle

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Functional imaging has shown that the basal ganglia are involved in the activity changes across the human sleep-wake cycle. Here we used frequency analysis to explore whether motor nuclei of the basal ganglia (Globus pallidus internus [GPI] and subthalamic nucleus [STN]) are functionally connected to the motor or the visual cortex in wakefulness, NREM2, NREM3/4 and REM-sleep. To this end, we examined patients undergoing deep-brain stimulation for Parkinson’s disease (PD; n=9) or dystonia (n=7). We simultaneously recorded local field potentials either from GPI or STN using a bipolar montage as well as scalp EEG (F3/4-C3/4, Pz-O1/2). Frequency analysis of scalp EEG between motor and visual cortex in GPI-patients confirmed previous studies in healthy subjects during sleep (Achermann & Borbély, 1998), whereas in STN-patients additional peaks were present in the 5-8-frequency range. In the coherence spectra strong peaks can be shown at 12–16 Hz between GPI and both motor and visual cortex in NREM2, corresponding to the sleep spindle frequency range. Further, a distinct peak could be identified in the higher a-range (10–12 Hz). In contrast, in NREM3/4 the 12–16 Hz-coherence peak disappeared while the peak at 10–12 Hz remained. For both NREM2 and NREM3/4 the 10–12 Hz-peak disappeared after partialisation of the surface EEG with GPI as the predictor, but not in STN patients. The directed transfer function (dtf) revealed that the peak at 12–16 Hz is predominantly propagated from the visual cortex to both GPI and motor cortex in NREM2 and NREM3/4. The dtf for GPI to motor and visual cortex showed a distinct peak in the higher a-range (10–12 Hz) in NREM2, while in NREM3/4 distinct peaks at 10–12 Hz were present between GPI and motor cortex in both directions as well as from motor to visual cortex. Principally, the same coherence patterns were also present between in STN-patients, however at a much lower level and less homogenously than in GPI-patients. There was no significant coherence in REM between STN or GPI and cortex. We can show functional connectivity of GPI and STN in NREM sleep between both the motor and the visual cortex in the frequency range of sleep spindles. The motor system seems to be additionally synchronised in the higher a-range (10–12 Hz) with the progression of NREM sleep, propagated through the GPI to the cortex. This higher a-peak is also present in STN patients, but the latter is not directly connected to the cortex. Most likely, the synchronisation at 10–12 Hz can be regarded as a specific signature of the motor system in NREM sleep, which parallels the synchronisation in the frequency range of sleep spindles.

O 120

Cerebral Blood Flow In REM Sleep: Is Oxygen a Key Regulator?

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Rapid-eye-movement (REM) sleep is remarkable for its high basal cerebral blood flow (CBF) which exceeds that in all sleep-wake states, and for the further CBF increases associated with transient blood pressure (BP) surges. It has been proposed that sensitivity of cerebral vessels to low PO2 is a fundamental property that determines the level of CBF (Zoccoli et al. 2002). If this were to be true, oxygen levels should be a powerful determinant of CBF in all behavioural states, though perhaps not predominant in REM. In specific tests of the hypothesis we: (a) contrasted the response of the cerebral circulation during REM and non-REM sleep to transient, episodic arterial oxygen desaturations designed to mimic sleep apnea (HYPOXIA IN SLEEP); (b) determined the changes of CBF associated with REM and non-REM occurring against a background of continuous hypoxia (SLEEP IN HYPOXIA); and (c) examined CBF increments during episodic blood pressure surges (REM SURGES) in normoxia & hypoxia. Lambs (n = 11) were instrumented to record beat-beat cerebral blood flow (CBF) using a 2 mm diameter TRANSONICS TM transit time ultrasonic flow probe implanted around the superior sagittal sinus, and implanted with catheters to record cerebral perfusion pressure (CPP) and electrodes to define sleep-wake states. Arterial oxygen saturation (SpO2) was recorded with a NELLCOR™ pulse oximeter. CBF was contrasted between REM and non-REM sleep occurring naturally during normoxia (FiO2 0.21) and during hypoxia induced by reducing FiO2 to 0.10 either (a) transiently (60 s) within individual sleep epochs (HYPOXIA IN SLEEP); or (b) continuously (1 hr) across repeated sleep epochs (SLEEP IN HYPOXIA). Under baseline (normoxia) conditions, CBF (ml/min) was significantly greater in REM than in non-REM (17 ± 2 vs. 14 ± 2, P < 0.05, mean ± SE, 2-way RM ANOVA). During continuous hypoxia, increases of CBF occurred in REM (24 ± 7%, P < 0.05) and non-REM (14 ± 5%, P < 0.05), and the greater CBF (ml/min) of REM (26 ± 3) compared with non-REM (18 ± 1) was preserved (P < 0.01). Similarly, there was preservation of the significantly greater CBF of REM compared with non-REM under conditions of transiently (60 s) imposed hypoxia. During BP surges (delta BP ~20%) peak CBF increased similarly in normoxia (23 ± 6%), continuous hypoxia (19 ± 13%) and transient hypoxia (22 ± 3%). As the major circulatory features of REM sleep (CBF in REM > NREM; large surges of CBF) are preserved in hypoxia, regardless of its duration, sensitivity of cerebral vessels to PO2 appears to be a fundamental property that powerfully affects the basal level of cerebral blood flow, but not the sleep-wake differences. Zoccoli G, Walker AM, Lenzi P, Franzini C. The cerebral circulation during sleep: Regulation mechanisms and functional implications. Sleep Med Rev, 6(6):443–455, 2002.

O 121
Effects of different illumination levels on visual performance, alertness and well-being in workers during day shift
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Introduction: Brighter light in the work place is expected to have positive effects upon vision, alertness, well-being and quality of work. We performed the study “Lichtdimensionen” during fall 2004 to investigate quantitative effects during work at daytime. At three illumination levels workers were examined directly at their work place with respect to visual acuity (VA), contrast sensitivity (CS), colour vision (CV), alertness, subjective perception and mood.

Methods: The local ethic committee approved this project and each participant gave his written consent.

Work place: Three production lines in the carcass finish of Mercedes E-Class.

Illumination: Fluorescent tubes (Philips TLS 80W/865). Levels tested: 500, 1500 and 2500 lux.

Subjects: 28 adult male subjects after screening for visual function, data of all study visits available in 25 subjects.

Time schedule and design: Examinations were performed in two blocks of four weeks each with two weeks break after the end of daylight saving time. Two groups of worker (A and B) were examined during early day shift (7 a.m.-2 p.m.). Illumination levels were alternating weekly (Table 1) with respect to expected effects of sequence and Hawthorne.

Table 1

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Tests: ETDRS chart (VA), Pelli-Robson chart (CS), Farnsworth 28 HUE -desat (CV), subjective visuelle analogue scales for contentness with illumination, mood,
well-being, alertness. Objective assessment of central nervous activation: Pupillographic Sleepiness Test (PST by AMTech, Germany).

Analysis: For all variables differences between conditions were compared by a one-sample t-test/Wilcoxon test. Correlations were determined according to Spearman.

Results: Neither the parameters of visual functions nor subjective scales nor objective alertness revealed differences between 500, 1500 and 2500 lux. These results were convincing and missed statistical significance by far.

Discussion: Visual functions at 500 lux could not be improved by rising the illumination level to 1500 or 2500 lux. Our results concerning subjective/objective alertness and well-being during early day shift are in contradiction to expectations from chronobiological human experiments with monochromatic light. But these were focussed on biological light effects with regard to the circadian phase. The results of a recent study about light effects during night shift have not yet been published. Actually, there are no recent studies directly comparable to the present one.

Acknowledgements: This trial was sponsored by *DaimlerChrysler AG, Sindelfingen, PWT/VBT, and initiated by Rainer Röck. We thank Alexander Baier and all foremen for excellent support and all subjects for their participation.

Children

O 122
Life quality & well being as sleep related factors in self-reports of school children between 11-15 years in the Vienna epidemiologic study

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Aim: Sleep disorders are recognized as an important cause of a wide spectrum of morbidity in children. Depending on the technique of surveys and the age of investigated cohorts, prevalence of pediatric sleep disorders varies widely. In an epidemiological study we determined the frequency of self-reported symptoms characteristic for lifestyle and well being, as well as for para-/ insomnia and obstructive sleep apnea (OSA), in school children between 11 and 15 years.

Method: The study was performed in 21 randomly selected schools in the Vienna area. Children’s questionnaire was developed in a pilot study, and consisted of 45 multiple-choice questions about the socioeconomic status, possible sleep disorders and signs or symptoms of obstructive sleep apneas (OSA). Parents’ questionnaire consisted of 8 questions and items like snoring, obstructed breaths and apneas.

Results: 1434 school children were interviewed by a questionnaire (mean age 12.5 years, median 13 years, 676 girls vs. 699 boys). On schooldays mean nocturnal sleep duration was 8:8h (median: 9.0 h; SD: 1:23; 4:30–12 h). Waking up times ranged from 5:00–7:45 (24.1%: <6:00 h: 29.6%: 6:00–6:30 h; 46.3%: >6:30); bedtimes from 19:00–1:00 (45.1%: <22:00 h: 29.7%: 22:00–22:30 h; 25.2%: >22:30). Waking up <6:00 h was associated with snoring and being grumpy in the morning. Bedtime >22:30 h was associated with increasing age, lifestyle, school performance, well-being, daytime constitution, and quality of life. 25.7% of investigated children slept <8.5 h; 41.9% slept 8:30-9:30 h, and 32.4% >9:30 h. Sleeping time decreased with age from 9:32h (11a) to 8:55 (15a; linear regression 0.25). Sleep duration was also influenced significantly by issues of lifestyle (i.e. TV, computer games, dinner time, cinema, café, disco). There was no influence on sleep duration by the time spent with sports, homework-writing, friends or alone, but the more time a child spend with his/her parents and siblings per day, the more he/she sleeps, and the worse the general wellbeing is, the less he/she sleeps.

Conclusion: Duration of sleep is influenced by age and life style; both influence daytime constitution, quality of life/ well being, and school performance.

O 123
Snoring as a sign of various sleep disturbances in school children between 11 and 15 years—results of the epidemiological study in Vienna

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Aim: The prevalence of snoring was evaluated in school children between 11 and 15 years of age. In addition to items reported by parents, children were asked to answer a questionnaire in order to receive information about the children’s potential complaints, school performance and life style.

Method: The study was performed in 21 randomly selected schools in the Vienna area. Children’s questionnaire was developed in a pilot study, and consisted of 45 multiple-choice questions about the socioeconomic status, possible sleep disorders and signs or symptoms of obstructive sleep apneas (OSA). Parents’ questionnaire consisted of 8 questions and was also used to calculate the Brouillette score from the items snoring, obstructed breaths and apneas.

Results: 1434 school children were investigated (mean age 12.5 years, median 13 years, 676 girls vs. 699 boys).
5.2% (74/1434) of children and 6.9% (86/1259) of parents or caregivers reported about snoring (frequently or very frequently). There were no sex differences. None of the children had a clearly positive result from the Brouillette score (indicating OSA), whereas “suspicious OSA” was observed in 3.2% (40/1259). When frequent and very frequent snorers were compared with the remainder, the snorer group showed more mouth breathing during sleep (p < 0.00001), mouth dryness (p < 0.00005), headache (p < 0.0005), cigarette exposition at home (p < 0.001), smoking (p < 0.005), daytime naps (p < 0.005), crying out of sleep (p < 0.01), daytime tiredness (p < 0.05) and a higher body mass index (p < 0.05).

**Conclusion:** In our study, the Brouillette score was unable to identify potential OSA as a main sleep disorder. Compared to other studies, the prevalence of snoring is lower in our study. Snoring seems to be a sign or symptom of various sleep disturbances and not only of OSA. A statistically significant correlation between snoring and anamnestic hints to various sleep disturbances underlines the need to ask concerned children themselves for observations potentially associated with sleep disorders.

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**O 124**

Pediatric Sleep breathing problems: a multidimensional scaling model

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**Study objectives:** Using a multidimensional scaling model we investigated the relationships between pediatric sleep disorders and daytime behavior in school age children with sleep breathing disorders (SBD).

**Method:** Validated questionnaires on nighttime behavior, daytime behavior, and respiratory health were filled out by parents of 3045 school children in Belgium. For this study children who met the criterion of having at least 1 sleep related breathing problem (3 or more times per week during the past 6 months) were selected for further analyses. Sleep problems, sleep efficiency, sleep environment, sleep enuresis, internalised and externalised behavioral problems, respiratory health of the child and relatives, smoking exposure, and caffeine consumption, or a total of 26 indicators were defined and modelled.

**Results:** 4.1% of the children were reported to have a SBD symptom. These children differed on sleep and health domains from non-SBD-children. In addition, through scaling of the (dis)similarities among the 26 indicators the SBD-child was able to be portrayed. That is, based on an internal analysis of the data-matrix, through elimination of sleep correlates, health of the family, and behavior rated by teachers, followed by caffeine intake, drugs, and behavior...
verbal learning and episodic memory all groups showed a similar learning curve comprised of three trials. Compared to the number of words learned during the rehearsal, number of remembered words in immediate and delayed recall declined more in the postmenopausal groups than in the young (P<0.001). No change was found between the immediate and delayed recalls. In addition, performance was impaired in all groups during sleep deprivation (P<0.001), but it returned to the baseline level after one recovery night (P<0.001). No main effect of hormone therapy was observed in either of the tests.

**Conclusions:** Sleep deprivation impaired verbal learning and memory similarly in postmenopausal and young women. In the easier verbal memory test practice effect was hindered during sleep deprivation, whereas in the more demanding verbal memory test performance declined. In general, postmenopausal women performed worse than young controls in all conditions. All groups showed recovery already after one recovery night. Thus, there is no difference between young and aging women in coping with sleep deprivation regarding verbal memory functions. Hormone therapy gave no advantage to the postmenopausal women.

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**O 126**

**Acute and long term adaptation of TSH to partial sleep deprivation and recovery**

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**Aims:** The main aim was to evaluate how the regulation of human thyroid stimulating hormone (TSH) adapts to partial sleep deprivation (PSD).

**Methods:** Nine subjects participated in a strict 6-week sleep protocol, in which subjects slept in the sleep laboratory for 12 days, Habituation (sleep 23-07h), Baseline (23-07h), PSD (03-07h) and Recovery (23-07h). For 9 of those days, blood was drawn every hour from 23-08h and every 3rd hour 08-23h.

**Results:** Mean TSH varied significantly across days (p<.001), across time within days (p<.0001), interaction between days and time (p<.001). Contrasts (p<.05) showed a significant: (1) acute increase of TSH during PSD between 23-03 (when subjects normally slept); (2) a gradual decrease across days with PSD; (3) a strong reduction during the first recovery day; (4) a return to normal on the second recovery day; and (5) a continued increase the 3rd recovery day above baseline.

**Conclusions:** There were potent acute effects on TSH regulation by sleep restriction—an increase-and of recovery sleep (8h)—a decrease. However, the strong acute effects were followed by a gradual adaptation to the new sleep pattern were TSH levels seemed to return to baseline Fig. 1.

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**O 127**

**Chronic Sleep Deprivation Produces Cognitive Deficits Similar To Those Seen In Restless Legs Syndrome (RLS) Patients**

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**Aims:** Cognitive tasks involving mostly pre-frontal cortical (PFC) activity have been shown to be sensitive to one-night sleep deprivation and also abnormal in untreated restless legs patients who have chronic sleep loss. The PFC tests have not been evaluated after chronic sleep loss similar to that reported by RLS patients. This study evaluates these tests using the same procedures for evaluating RLS patients and control subjects without sleep loss.

**Methods:** 8 normal controls selected to match education level and age of previously tested RLS and control patients slept 6 hours or less for 2 weeks and were then given cognitive tests in the morning after the last night of sleep restriction. The tests and procedures were identical to those used to assess 15 age-matched controls without sleep restriction and 16 RLS patients. The tests chosen included primary PFC tests (2 verbal fluency tests and a trail making test), general non-verbal cognitive tests (Porteus Mazes and Stroop Color Word test, and Colored Progressive Matrices test). The verbal fluency tests lasted only one minute and were naming words that began with a specific letter (repeated for 3 separate letters F, A and S) and naming words that belong to a specific category (repeated for 3 categories: animal, vegetable and fruit). The short duration tests reduced confound from sleep-loss impairment of ability to maintain attention.

**Results:** ANOVA for group (sleep restricted, normal sleep and RLS) and sex showed significant group effects (p<0.05) for both verbal fluency tests but not for the other tests. There were no significant sex effects. The post-hoc analyses showed no significant difference between RLS and sleep restricted (p>0.10) but significant (P<0.013)
differences between both these groups and normal sleep controls for the category verbal fluency and significant differences between sleep restricted and non-restricted controls for the first-letter verbal fluency tests (p < 0.027). The sleep restriction produced a significant 30 to 33% decrease in verbal fluency test performance similar to that seen in RLS patients. The CPM tests had nearly identical scores for all groups suggesting no difference in overall cognitive abilities.

**Conclusions:** These data show that chronic sleep loss similar to that reported for RLS produces similar and clinically significant PFC deficits found with one night total sleep loss. The RLS patients show the same deficits indicating that untreated RLS patient have significant cognitive deficits that result largely from their chronic sleep loss.

**O 128**

Visual perceptual impairments and flight performance decrements in pilots begin at 19 hours of continuous wakefulness

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**Aims:** Visual neglect phenomena have been demonstrated in acute sleep deprivation and correlated with flight performance in pilots (1). The aims of this abstract are to discuss visual perception, simple reaction time, and flight measures collected from pilots in an air-refueling simulator (ARPTT) over 26.5 hours of continuous wakefulness.

**Methods:** Eight military pilots (m, 31–52 y/o, mean 37yrs) on flight status were recruited to perform the primary task of flying a simulated 12.5-hours overnight mission after a day of continuous wakefulness, and perform the secondary task of responding to repeated 20-minute presentations of single- and double-light stimuli displayed in random sequence in an arc 75-degrees-left to 75-degrees-right of center of the head. The Choice Visual Perception Task (CVPT) consisted of 150 stimuli, each 0.25 second in duration, presented while the pilot maintained airspeed of 275 knots immediately behind and below the tanker. On study test day the subjects remained active throughout the day and at 8 pm began a 12.5-hour simulated flight. Complex performance was measured through deviations from a pre-established azimuth heading during the visual perception task. The flight heading impairments were captured during four 15-minute refueling periods. Simple reaction time was measured using the Psychomotor Vigilance Task (PVT) during crew rest periods. Analyses are final.

**Results:** Significant visual perceptual impairment, significant complex motor performance impairment, and significant simple reaction time decrements (PVT) each began during the 19th hour of continuous wake (at 0100 clock time). Visual perception impairments (CVPT response omissions) significantly correlated with flight heading impairments at r=0.97 and with PVT speed at r=−0.92. Flight heading impairments significantly correlated with PVT speed at r=−0.92 and lapses at r=0.91.

**Conclusions:** Impairments on a choice visual perception task, a simple reaction time task, and on a complex motor flight performance task began at 19 hours of continuous wake. The implications are that acute sleep deprivation can impair both visual perception and motor performance at an earlier time than many individuals may be aware. The take home point is that small amounts of sleep deprivation, considered moderate or minimal by many healthy members of society, can significantly impair motor performance.

**Reference**


**Behaviour and Dreaming**

**O 129**

Low-resolution brain electromagnetic tomography reveals cortical reactivation during spindle episodes in a night following paired word associate learning

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**Objectives:** Experience-dependent cortical plasticity observed during posttraining sleep has been hypothesized to be part of the global process of memory consolidation. Low-resolution brain electromagnetic tomography (LORETA) offers the possibility of investigating under normal (undisturbed) sleeping conditions when (in which sleep stages) and where (in which cortical brain regions) experience-dependent reactivation occurs. Recent studies suggest a connection between explicit memory tasks and the activity of sleep spindles in the night following learning.

**Methods:** Twenty four young healthy volunteers spent 3 nights in the sleep-lab. After an adaptation night subjects were randomly assigned in the 2nd and 3rd night either to a control condition without intentional learning or to an experimental condition (declarative memory task, paired-associate word list, 160 word pairs, 2.5 hours before sleep).
Subjects performed cued recall in the evening and in the following morning. Spindles were detected automatically by means of the Somnolyzer 24×7 and LORETA was applied to 2-s spindle as well as non-spindle epochs in stage 2.

Results: Changes in spindle intensity (experimental minus control night) were significantly correlated to overnight changes in memory performance ($r = .52, p < .01$). These correlations were most prominent in the first three 1.5-hours parts of the night. Changes in memory performance correlated significantly only with fast but not with slow spindle measures. Correlation analyses between changes in LORETA spindle power and memory performance demonstrated significant negative correlations at 13.2 Hz in the right medial temporal lobe (including hippocampus proper), the fusiform gyrus, the temporal (BAs 21,22) and frontal lobe (BAs 6,9,10) and in the cingulate gyrus (BAs 24,32).

Conclusions: The intensity of fast, but not of slow spindles during S2 sleep was significantly correlated to declarative memory performance. LORETA revealed positive correlations in the fast spindle frequency band exclusively in brain regions whose activity-as shown by PET studies-is associated with how well declarative memory tasks are performed. Thus, the present study directly proves the involvement of sleep spindle activity in the consolidation (enhancement) of explicit memory.

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O 130

Dreams and psychological adaptation

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Among many functions of dreams most authors stress as the most important one-the function of psychological adaptation. In order to study defensive function of dreams we have examined 198 patients with neurotic disorders and 55 healthy subjects. The multiple recordings of dreams were carried out by taping the subjects dream reports immediately after morning awakening.

In each case a stage of neurotic state was defined: either compensation or subcompensation or decompensation. Various methods of dream research developed by us were used. There are: the method of Dream Content Analysis, which allows to evaluate frequency, character and structure of dreams and analysis of dream as a model of stress situation (analysis of way of getting out of dream culmination).

At the earlier stage of the disease we have noted the following changes: increasing dream intensity and activating affective experiences (high frequency of emotional reactions during the dream) and complex changes in dream structure as well.

In phase of decompensation dreams activity intensification was followed by its depression (low frequency, rare connection between waking up and dreams), keeping negative emotional background.

In the group of patients with neurotic disorders in comparison with healthy subjects negative way of getting out of culmination of dreams in cognitive (negative interpretation) as well as in affective (negative emotion) spheres and active leaving in behavioral level, were predominant.

So, peculiarities of psychological adaptation are reflected in dream content.

O 131

Sexual Behavior While Asleep—Medicolegal Consequences

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Introduction: Parasomnia involving sexual behavior is more frequent than previously thought, consisting of several distinct features that distinguish it from sleep-walking. State-dependent, sleep related sexual acts are an important concern of forensic sleep medicine, yet have been rarely reported and clearly not systematically addressed. Determining the state-dependent nature of a sexual act is predicted upon comprehensive multidisciplinary sleep evaluation that utilizes specific protocols. This presentation will review the protocols and the available electrophysiological monitoring means that must be included in such an evaluation.

Methods: Using three selected cases, (a) alleged nighttime rape of a spouse in the couple’s bedroom; (b) alleged sexual assault of a teenagers by another teen sleeping in the immediate vicinity; and c) alleged sexual fondling of a child by an adult while napping in bed, the author will present his findings on sleep related phenomena such as sleepwalking, night terrors, confusional arousal, REM behavioral disorder, nocturnal seizures, and dissociative states originating in sleep that can be potentially associated with violence. Specific references to the comprehensive protocols used to answer the question of sleep related sex, both medically and legally, and how they pertain to these cases, will be discussed.

Results: The legal outcomes of these cases differed significantly and demonstrate that the question of sexual act/assault carried out allegedly in the sleep state requires a careful, thorough and systematic work-up. Clinicians must follow clearly defined scientific methods to limit the risk of opening a Pandora’s box of unsubstantiated precedence or wrongly convicting a legitimate case of an action that might
not have been carried out with the individual’s conscious awareness.

**Conclusion:** Utilizing sleep related science and guidelines, sleep experts can assist the medico-legal system in assessing for the possibility of sleep related sexual behavior. The forensic implications of this question, including directions for future research will be discussed.

**O 132**

**Is there a link between Cyclic Alternating Patterns and Sleep quality?**

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**Introduction:** The aim of the study was to examine the relationship between subjective and objective sleep quality of good sleepers. Besides standard polysomnographic (PSG) parameters for sleep quality also Cyclic Alternating Pattern (CAPs), a periodic EEG activity of nonREM-sleep were identified visually by two independent scorers.

**Methods:** Twenty eight healthy sleepers, aged between 21 and 86 years (20-39 years: n = 8; 40-59 years: n = 8; > 60 years: n = 12), underwent PSG-recordings of two consecutive nights. Sleep EEG-analysis was performed according to the standard scoring rules for sleep stages (Rechtschaffen & Kales based visual sleep scorings) as well as for CAPs (according to the rules of Terzano et al., 2000).

**Results:** The sleep architecture of the adaptation night was compared to the baseline night to determine those parameters, which differ over the two nights. Besides REM-latency and the CAP rate (=time spent in CAP cycles in relation to the time spent in nonREM-sleep) no significant differences between the two nights were found. Subjective ratings of sleep and awakening quality (as measured by the self assessment scale for sleep and awakening quality [SSA]; Saletu et al., 1987) did not differ between the two nights but mood, affectivity and drive as measured by visual analogue scales show significant differences. Therefore, the dimensions “active-passive” and “wake-tired” as subjective ratings of sleep quality and the CAP rate as an objective criterion were compared. In young adults (20 to 39 years) a significant negative correlation for the dimension “active-passive” was found in both nights (1st night: -0.778; p = 0.023. 2nd night: -0.909; p = 0.002) but not for elderly (>40 years). All other examined parameters (sleep efficiency, latency, distribution of sleep stages, subjective ratings of sleep and awakening quality) are not correlated with CAP variables.

**Conclusion:** These results confirm already published data about cyclic alternating patterns, whereby the CAP rate can be considered as a criterion for objective sleep quality.

**O 133**

**The Effect of Daytime Naps on the Recall of Verbal Material**

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**Aims:** It was recently shown that diurnal naps may positively influence the performance at a procedural memory task, to an extent similar to the one obtained with a whole night sleep. This study is aimed to investigate whether naps could also be beneficial to a declarative memory task.

**Method:** Twenty five healthy young subjects (M = 3, F = 22, age range 21-27) were asked to learn a list of 20 non-associated word pairs. Immediate recall was required immediately after presentation (T0, h14.00), after a two-hours retention interval (T1, h16.00) and at a further point in the early evening (T2, h19.30). Thirteen subjects spent the retention interval awake, (condition W) whereas to other twelve subjects, in the same interval, a nap was administered (condition N) and polysomnographically recorded. Sleepiness at each recall test was controlled by means of the Karolinska Sleepiness Scale.

**Results:** In N, total sleep time was 82±36 min, with sleep efficiency 63.7±24.0%. NREM sleep proportion was 89.8±5.0%, while REM proportion was 10.2±7.6%; five out of fourteen naps contained less than 5 minutes of REM sleep. ANOVA did not show significant changes across time of the memory scores within each group, but detected a significantly different profile between the two groups (N = 6.5±2.8, 6.6±2.6, 6.6±2.7 vs. W = 4.7±2.3, 3.8±1.8, 3.5±1.7. Ftime = 0.3, ns; Fcondition = 8.98, p = 0.006; Ftime×condition = 1.77, ns). Recall scores show an improvement across time after naps containing at least 5 minutes of REM sleep (napREM: 7.1±3.0, 8.3±4.1, 8.8±3.3, F = 4.56, p = 0.03).

**Conclusions:** Daytime naps turn out to be partly beneficial for declarative memory since they prevent the forgetting of material going on in the waking condition. Furthermore, although no such an increase as the one described for procedural memory tasks1, was globally observed after naps, an actual improvement of the scores regards those naps containing a minimum amount of REM sleep. That might be linked to the build up of a complete sleep cycle, whose role for declarative memory has been recently put forward 3,4.

O 134
The Effect of Napping on an Implicit Memory Task

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Aims: Sleep has an important function in memory consolidation. Both, early slow wave sleep (SWS) and late rapid eye movement (REM) sleep are required for overnight learning (two-step model of memory consolidation). SWS is more important for explicit, while REM sleep is more relevant for implicit memory consolidation. The present study tested whether napping in the afternoon, for less than 90 minutes, has a positive impact on an implicit memory task compared to active wakefulness, and whether REM sleep is necessary for implicit memory consolidation.

Methods: Preliminary results from 20 healthy young subjects (13 female, 7 male; aged 23.5±2.9 yrs) are reported. All subjects filled in a sleep log and were monitored by actigraphs for 14 days. On day 7 and day 14 subjects learned to perform a mirror tracing task or a control task (cross-over design) in 2 encodings and 1 retrieval trial between 11:00 and 13:00h. The “mirror-tracing task” consisted of 12 stimuli (Plihal & Born J. Cog. Neurosci 1997; 9: 534-547). Subjects had to trace each figure with an electronic stylus looking in a mirror. The speed of tracing, error counts and error time were averaged. Subjects were randomly assigned to either a nap or an active wakefulness group (listening to radio dramas) between 14:00 and 15:30h. In a 2nd retrieval trial performance in the mirror tracing task was checked 45 minutes thereafter.

Results: All subjects in the nap condition were able to sleep on both nap opportunities. Mean total sleep time of all naps was 69.9±10.5 minutes, mean sleep efficiency was 77.6±11.6%, and the mean sleep latency was 12.6±4.8 minutes. Performance of the two conditions (nap/no nap) did not differ during the two encodings and the 1st 4.8 minutes. Performance of the two conditions (nap/no sleep is necessary for implicit memory consolidation. The present study tested whether napping in the afternoon, for less than 90 minutes, has a positive impact on an implicit memory task compared to active wakefulness, and whether REM sleep is necessary for implicit memory consolidation.

Conclusions: Napping improved memory consolidation in an implicit memory task. Subjects, who reached REM sleep during napping did not differ in the performance scores compared to those, who did not show any REM.

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O 135
Sleep spindle activity in the human EEG and their interaction with “general learning abilities”

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Aims: In the last few years the sleep and memory consolidation hypothesis has triggered massive and renewed research interests focusing (primarily) on the significance of different sleep stages for memory processes. More recently, also stage 2 sleep with sleep spindle activity as a central feature has been proposed as a possible candidate for improving overnight performance in different memory tasks (cf. Schabus et al., 2004). Additionally, it is discussed if sleep spindle activity might also be related to general learning abilities or “intelligence” (cf. Nader, R., & Smith, C. In P. Maquet, C. Smith, & R. Stickgold (Eds.), Sleep and brain plasticity (pp. 87-98). New York: Oxford University Press, 2003). The present work aims to shed light on this issue by examining various sleep spindle parameters possibly related to “general learning abilities”.

Methods: Forty-eight students (between age 20 and 30) were randomly assigned to either (i) an implicit/procedural mirror tracing task or (ii) an explicit word-pair-association task and slept in the sleep laboratory three times (screening/adaptation, experimental, control) over the course of a month. Before assignment all subjects were tested on various psychometric tests including the Wechsler Memory Scale (WMS-R) and the Advanced Progressive Matrices (APM). Spindle detection throughout the night (approx. 8 hours) was based on a new and refined automatic algorithm (cf. Anderer et al., 2004) which provides specific sleep spindle features (duration, amplitude, frequency, number of detections) and thus reflects the activity or intensity of the spindle process.

Results: Over the course of the night(s) the number as well as duration and amplitude of automatically detected (‘slow’ and ‘fast’) sleep spindle revealed significant associations with “general measures of learning ability”. Using (spindle) event-related synchronization/desynchronization these effects are visualized and depict the massive spindle-related synchronizations in the sigma frequency band.

Conclusions: The data thus suggests that human sleep spindle activity might not only be related to processes involved in memory consolidation but “general learning abilities” alike.

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Other Sleep Disorders

O 136
Importance of the otolaryngologist examination in sleep apnea patients
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Introduction: The upper airway is the main anatomical site responsible for obstructive sleep apnea. We studied whether the otolaryngologist examination could predict the severity of Obstructive Sleep Apnea.

Material and Methods: 201 patients were included in this study. We did a complete examination of the nose and pharynx. We also studied the Body Mass Index, neck circumference and performed complementary examinations (rhinomanometry, cefalometry, functional study of inferior airways, and polygraphy), but in this study we only commented on the otolaryngologist's findings and their relationship with the polygraphy. In the exam of the pharynx we considered these different parameters: Mallampati Modified Index (mouth open and without protrusion of the tongue), tonsils, uvula, and the Muller test. All data was studied with the SPPS 11 regression model.

Results: The mean age was 52, between the ages of 19 and 80, with 47 women and 154 men. We observed a statistical correlation between the Modified Mallampati Index (P<0.01) and tonsils (P<0.03) and the results of Apnea-Hipopnea Index. We didn't find a relationship with the other parameters studied—uvula (P<0.125), Muller test (P<0.176), neck circumference (P<0.206), nasal resistance (P<0.286)—and the results of the Apnea-hypopnea index.

Conclusion: We concluded that although the size of tonsils is related to the severity of apnea-hypopnea syndrome, the Mallampati Modified Index is more highly predictive.

O 137
A proposed classification for leg movements during sleep based on recording of multiple muscle groups
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Aims: Leg movements during sleep were first described in 1953 and recorded on an overnight polysomnogram in 1965. Since that time only the anterior tibialis muscle has been recorded routinely in clinical overnight sleep studies and standard criteria for the diagnosis of periodic limb movement disorder (PLMD) have been established. However, the clinical significance and site of origin of the movements is still being debated as is their relationship to arousals and sleep stages. A more comprehensive system is required to assist in solving these problems.

Methods: Ten patients with restless legs syndrome were recorded overnight with surface EMG electrodes over the anterior tibialis, gastrocnemius, quadriceps and hamstring muscle groups of both legs. All leg movements occurring during sleep without regard for current PLMD criteria were analysed and classified according to their order of muscle activation.

Results: A total of 2100 leg movements were analyzed. A classification system is suggested which differentiates between concurrent or sequential muscle activation as well as total length of activation sequences. Activation sequences are divided into classes dependent on number of muscle groups involved. Preliminary data indicates changes in the number of sequences within different classes between sleep stages as well as different frequency distributions for the various classes.

Conclusions: The classification system is useful and lends itself to comparison with other EMG activation patterns particularly those occurring during wakefulness such as during the suggested immobilization test. These comparisons may assist in the localization of the site of origin.

O 138
Myoclonic head jerks in REM sleep are common in a sleep laboratory patient population
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Aims: Myoclonic events are common in wake-sleep transition (hypnic jerks). During REM sleep movements are rare because of physiologic muscle atonia, but both random myoclonic twitching and sleep myoclonus are well known phenomenons during REM sleep. We intended to quantify the occurrence of myoclonic jerks in REM-sleep and focused on head jerks since these movements are readily identified in EMG and videographic recording.

Methods: We examined REM sleep of all patients admitted to our sleep laboratory in a course of six months in order to detect the number of myoclonic head jerks. From January to June 2004 205 patients underwent polysomnographic recording (one to four nights). 147 patients (71.7%) were men, 58 (28.3%) were women, mean age was 50±14.4 years (range 14–82). The principal sleep related diagnosis was sleep disordered breathing in 136 patients, Restless Legs Syndrome/Periodic Limb Movements in 12 patients, insomnia in 16 patients, narcolepsy in 5 patients, and other sleep diagnosis in 36 patients. REM sleep was examined visually in the PSG (occurrence of movement
artifacts or myoclonic muscle activity) and by video (head jerks) by one scorer. Head jerks were only scored when the movement was visible in the video.

Results: 472 nights of 205 patients were analyzed. 112 patients (54.6%) had head jerks during REM sleep, 93 patients (45.4%) did not show head jerks. Patient with head jerks had a mean of 3.29 ± 5.16 (range 1-44) jerks during REM sleep. We compared the occurrence of head jerks in different age groups. In the youngest patient group aged below 45 years (n=72) head jerks were detected in 46 patients (66.7%), in the group between 45-60 years (n=72) head jerks were present in 39 patients (54.2%) and in the oldest patient group above 60 years (n=61) head jerks were seen in 25 patients (41%). The association between head jerks and age was significant (chi-square test, p=0.012).

Conclusions: Our data confirm previous observations that head jerks are frequent in REM sleep and might represent a physiological phenomenon. Furthermore a significant difference in the occurrence of head jerks in different age groups was observed with a higher prevalence in younger individuals.

O 139
Quality of life in case of sleep apnea syndrome
and neurological disorders

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Introduction: Apart from a multitude of physical complaints, both the obstructive sleep apnea syndrome and neurological disorders can also lead to forms of mental illness, and the latter to a reduction in quality of life (QoL) and in the ability to subjectively perceive it. In such cases, different parts of QoL may be affected. Important factors in this can be the severity of the disorder on the one hand, and the duration of prior therapy on the other hand. The objective of this study was to investigate the degree of quality of life achieved both by patients with obstructive sleep apnea syndrome (OSAS) and by neurology patients.

Methods: The study was carried out involving two groups of randomly selected patients, one of OSAS patients and one of neurology patients, and healthies. During admission to the clinic, all patients were selected according to their clinical diagnosis (ICD-10):

1. For this purpose, a polysomnography according to the criteria of the DGSMS was carried out to arrive at a diagnosis for patients with OSAS (AHI: 33.9/h ± 21.2/h; mean AH duration: 53.9 s ± 30.2 s; SaO2min: 81.3% ± 6.7%).
2. During admission to the clinic, all neurology patients are examined neurologically and neuropsychologically. All test persons must not suffer from any severe psychiatric disorders.

So far, data have been gathered for 40 healthies (25 males; 15 females), 41 OSAS patients (37 males; 4 females) (before starting therapy and after 3 days of nCPAP therapy) and 132 neurology patients (76 male; 56 female) (with various neurological clinical pictures), using a sample of questionnaires, consisting of 4 questionnaires (among which a Patient Questionnaire and one concerning specific areas of their quality of life, München Lebens qualitäts-Dimensionen-Liste MLDL-Z).

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of tps</th>
<th>Mean age</th>
<th>AHI</th>
<th>Barthel Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthies</td>
<td>40</td>
<td>42.1 ± 12.1</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>OSAS patients</td>
<td>41</td>
<td>53.6 ± 13.0</td>
<td>33.9/h ± 21.2/h</td>
<td>–</td>
</tr>
<tr>
<td>Neurology patients</td>
<td>132</td>
<td>65.2 ± 13.3</td>
<td>–</td>
<td>81.3 ± 22.6</td>
</tr>
</tbody>
</table>

The study design intends for a comparison between these groups of patients and healthy persons. Further, the influence of the degree of severity on quality of life achievements (OSAS and neurology patients) and of the duration of CPAP using (OSAS) is to be examined.

Findings: Testing of quality of life achievements revealed a highly significant difference between healthy persons and OSAS patients, also difference between healthy persons and neurology patients.

Examination of specific areas of quality of life, 2 (of 4) subscales (physical QoL: p < .001; psychological QoL: p = .002) of the MLDL-Z showed significant to highly significant differences in OSAS patients and 4 (of 4) subscales (p < .001) of the MLDL-Z showed significant to highly significant differences in patients with neurologic disorders. In all dimensions of their quality of life, untreated patients (OSAS and neurologic patients) had lower scores than those who had undergone therapy.

1. Already after 3 days of nCPAP therapy, the OSAS patients’ quality of life tends to improve to a significant degree (p < .085). The catamnesis examination under long-term nCPAP therapy (>6 weeks) for OSAS patients improve to a significant degree (p < .05).

2. After 3 weeks of neurological rehabilitation, the neurologic patients’ quality of life improve to a significant degree (p < .05). The comparison between different clinical pictures of neurological disorders concerning quality of life is yet to be carried out.

Analysis of the degree of severity doesn’t show for OSAS patients (p > .05), but it shows for neurology patients that on the whole, there is a significant difference concerning quality of life achievements.

Discussion: The study revealed that both patients with obstructive sleep apnea syndrome and neurology patients show problems and deficits concerning their quality of life achievements. In contrast, the degree of severity of the
disorders is only relevant in neurology patients, but not in OSAS patients.

The OSAS patients’ quality of life improved already after 3 days of nCPAP therapy, but long-term nCPAP therapy is imperative to restore a healthy level.

In summary, based on our results, it is to be said that although continuous therapy improves the symptoms of sleep apnea syndrome and the neurological symptoms complex, quality of life achievements require longer-term degeneration.

O 140
Obstructive Sleep Apnea in Children with Down Syndrome

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Aim: To screen the prevalence of sleep-disordered breathing in a random sample of children with Down syndrome in Gaza City, Palestine

Patients: The study population included 77 (60 males and 17 females) consecutive children with Down syndrome mean age, 6.8 [4.5] years; range, 1-14 years). Methodology: physical examination, and lateral radiographs of the nasopharynx, hospital oximetry in The department of E.N.T. balsam Hospital-Palestinian Medical services, Gaza, Palestine.

Results: The prevalence of Obstructive sleep apnea was 57.1%, with a significantly higher prevalence in boys (61.6%) than in girls (35.2%). The group with sleep-disordered breathing was significantly younger (6.4 [3.9] years) than those with normal oximetry (9.6 [4.6] years). In the multivariate analysis, age (less than 8 years old), male sex and tonsillar hypertrophy were significantly associated with sleep-disordered breathing. Body mass index, adenoid hypertrophy, heart disease, malocclusion, and macroglossia did not affect the prevalence of sleep-disordered breathing.

Conclusions: The prevalence of sleep-disordered breathing in children with Down syndrome is very high, particularly in boys. Tonsillar hyperplasia may play a role in the pathophysiology of sleep-disordered breathing in these patients. Adenoid hyperplasia, obesity, and congenital heart disease were may have a role but not important risk factors for sleep-disordered breathing.

O 141
A new approach towards sleep: an ayurvedic point of view

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Pune/IND

Sleep is a natural urgency (or tendency) which everybody is exposed to. It is a type of “conditional reflex action” according to modern medicine, mostly linked with third ventricle and hypothalamus. In western medicine it is considered as a neurological event in which brain through sensory organs detaches from the external subjects. The disturbance in sleep is mostly considered as due to neurological or psychological origin. This is true up to a certain extent. Still it doesn’t help in providing satisfactory solution for the disturbance in sleep. Hundreds of medical research workers of different countries and different disciplines are working on this, but their efforts are sometimes inadequate or fall short of what they are aiming at. One aspect in sleep disturbance is mostly neglected: it can be a natural form (“constitutional”) rather than a disorder one, i.e. certain population has a tendency towards sleep disturbance though they are completely normal on all grounds. So such types of body constitutions need to be identified and consequently need to be considered with a specific approach. Hyperactivity, tiredness, degenerative pathologies and traumatic conditions are other known risk factors in sleep disorders. However, physiological process - or metabolism- seems to play an important role in the process of sleep. For example hyperacidity or acid peptic disorders, flatulence, constipation, intestinal disorders as well as fasting are known sleep disturbing factors. Whereas normalcy of intestinal and stomach functioning in digestion or metabolism maintain the normalcy and sound sleep. Now how to overcome sleep disorders and maintain the normalcy of sleep are the key questions. Ayurved (indian traditional medicine) have some views to offer to solve this problem. According to Ayurved sleep is a “mind game” in association with physiological elements. So by treating physiological imbalances along with maintaining the “rhythm of mind” could the sleep disorders be controlled. A study carried out in Ayurveda Department and Research Centre, Pune, India, shows that 43% of patients suffering from sleep disturbance are having problems related to digestion whereas 21% had this due to their natural tendency-without having any neurological or physiological disorder. A simplified treatment with external applications of oils and ghee (clarified butter) and intake of fatty food like buffalo milk gave encouraging results up to 73% among the suffering subjects.

O 142
The burden of disease in Restless Legs among members of a patient association

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Aims: Restless Legs is a common but still misunderstood neurological disorder with great impact on sleep. We aimed to estimate the impact of this disorder on social aspects of quality of life.
Methods: A self devised questionnaire containing questions related to various social aspects was distributed to the members of the Swiss restless legs patient association.

Results: 149 questionnaires could be collected and analysed. 51% reported to attend less often social activities such as visiting a theatre or cinema and 39% have changed their travelling methods or try to avoid travelling at all due to restless legs. 14% have changed the work to part time or switched to another job. The quality of life was also impaired by changes in character: 30 to 40% reported an increased nervousness, more frequent mood changes and impatience. 25% became depressive and 20% quick tempered. Also the delay of the correct diagnosis (mean 8.8 years; median 2.2 years) contributed to the burden of disease. The most frequent “wrong” diagnosis from a patients view were venous disorder (27%) or psychogenic disease. The most frequent “wrong” diagnosis from a patients view were venous disorder (27%) or psychogenic disease. The diagnosis was made in 50% by the patient him or herself after reading a newspaper or after a TV presentation.

Conclusions: Restless legs affects many aspects of quality of life in up to 30 to 50% of the patients in a severity forcing changes in social life and partly this is due to wrong or delayed diagnosis by the medical community.

O 143
Nasal (CPAP) compliance can be improved by simple interventions

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Aim: To test immediately OSA patients responds to CPAP treatment options Treatment options for patients with OSAS, include behavior modification, sleep positioning, diet program, (CPAP), surgical procedures as UPPP, LAUP, and jaw adjustment techniques. CPAP has been proven as a very effective treatment option for patients with OSAS, include behavior modification, sleep positioning, diet program, (CPAP), surgical procedures as UPPP, LAUP, and jaw adjustment techniques. CPAP has been proven as a very effective treatment option for OSAS. However, studies shown that patient’s compliance with CPAP treatment up to 70%.

Methodology: 201 patients with diagnostic of OSAS underwent a manually CPAP titration at the sleep lab between Dec. 2004 until April 2005.-170 followed by 12 days in average adjustment at home. Before and through the adjustment period patients received technical and medical support from the sleep lab technician and the CPAP Company. Solutions were offered according to the complain.

Results: 91 /170 (53.5%) after the adjustment period continued in daily nasal CPAP treatment. —79/170 (46.47%) patients had difficulties to adjust to the treatment because of financial, psychological, suffer also from Insomnia needed more time to adjust and other reasons.

Conclusion: The adjustment period is important for the patient and for the physician as well and simple intervention can improve CPAP compliance in new users. We conclude that CPAP titration and handling should not be left to home-care product companies it is depending on the sleep-lab technicians/coworkers.

O 144
When is sleep perceived as sleep and when as wakefulness?

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Aims: Electrophysiologically defined sleep is sometimes perceived as wakefulness, when subjects are deliberately awakened and interviewed. The probability of such a discrepancy between measured and perceived sleep depends on the current sleep state with more wake estimates after stage 2 (S2) than after REM sleep awakenings. One reason for this may be more dream-like cognition during REM sleep and more thought-like cognition during NREM sleep. The objective of the study was to assess differences in mental content when the experienced state was concordant or discordant with the electrophysiologically defined sleep state before the deliberate awakening.

Methods: 68 subjects (43 w and 25 m, mean age 24.1 years, SD=5.1 years) without sleep complaints were polygraphically recorded for one night in the sleep lab. Subjects were deliberately awakened by a tone signal (70 db) after at least 15 minutes of continuous S2 or 7.5 minutes of REM sleep. A standardised interview was performed with questions about state perception, different aspects of orientation, and mental content before the awakening. 39 subjects were awakened only once, either out of S2 or REM sleep, while the remaining 29 subjects had two awakenings (S2 and REM sleep) in randomised order. In case of two awakenings only the first one was regarded for the present analysis.

Results: About one third of the subjects rated the state preceding the awakening as wake instead of sleep. The proportion of wake judgements tended to be higher in S2 than in REM sleep (38.2% vs. 20.6%, chi square = 2.55, p = .11, n.s.). 80% of those subjects who perceived the state before the awakening as wake reported that they were oriented before the awakening, while this was the case in only 33.3% of those subjects who rated the prior state as sleep, with no difference between S2 and REM sleep. Finally, those subjects who reported having slept when
awakened from REM sleep had more image-like and uncontrollable mental content than those who reported being awake. Mental activity was higher in REM sleep (85.3%) than in S2 (64.7%) (chi square = 3.8, p < .05). Additionally, it was clearer in REM sleep than in S2 (64.7% vs. 23.5%, chi square = 4.8, p < .05), and it was more image-like in REM sleep than in S2 (70.6% vs. 23.5%, chi square = 8.54, p < .005).

Conclusions: The results show that state perception cannot be sufficiently explained by electrophysiological criteria alone, but seems also to depend on the degree of orientation and the quality of mental content. Sleep perception was positively correlated with image-like and uncontrollable mental content as well as with low external orientation, while wake perception was correlated with the reverse pattern. We suggest that subjects with a high degree of awareness in combination with wake-like cognitive activity perceive their state as wakefulness, even when they are sleeping according to electrophysiological criteria.

Animal Models

O 145
Cerebral sympathetic nerve activity increases during REM sleep
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The cerebral circulation is richly invested with sympathetic nerves arising out of the superior cervical ganglion (SCG). Previous studies have shown that increases in arterial blood pressure (ABP) results in increased sympathetic nerve activity (SNA) from the SCG and removal of the SCG lowers baseline cerebral vascular resistance (CVR) and significantly increases cerebral blood flow (CBF), yet the exact role of the sympathetic innervation of the cerebral circulation during sleep remains uncertain. Rapid increases in SNA, through vasoconstriction may protect the cerebral circulation during sleep against increased distending pressure in sleep, such as during the large transient rises in arterial blood pressure that are common in REM.

Conclusions: The role of the sympathetic innervation of the cerebral circulation from increases in ABP that occur naturally allowing tests of the hypothesis that SNA plays a protective role in the cerebro-vascular bed during natural arterial pressure surges. Lamb (n=2) were instrumented under general anaesthesia for recording of femoral arterial blood pressure and determination of sleep states (bio-electrodes). SNA was measured using 25 micrometer tungsten micro-electrodes, with a 1 mm bared tip inserted into the SCG. The signal was differentially amplified and filtered at 100-2000 Hz, and stored (sampling rate 10 kHz) for online spectral analysis. Substantially increased SNA (average 30 ± 7%) was recorded in the SCG as ABP rose acutely (average 41 ± 6%) during REM sleep (n=7). Bilinear regression analysis of these data show an increase in SNA preceding the rise in ABP by 5 seconds. These studies provide preliminary evidence for a potential protective role for the sympathetic innervation of the cerebro-vascular bed against increased distending pressure in sleep, such as during the large transient rises in arterial blood pressure that are common in REM.

O 146
Sleep apnoea features modelled by c-Fos proved brainstem mechanisms of gasp-, or hiccough-like aspiration reflex in cats
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Aims: (1) Animal model was developed to study the arousal and cardio-respiratory and neuro-physiological features of sleep disordered breathing (SDB) in patients. (2) C-Fos gene as an indicator of neuronal activity has been used to localise the brainstem mechanisms of so-called aspiration reflex (AR) induced by nasopharyngeal stimulation, resembling gasp, sniff or hiccough (Tomori Z, Widdicombe JG: J Physiol. 1969).

Methods: Fos like immunoreactive (FLI) dots were counted in brainstems from 11 cats (6 performing about 300 AR in 30 min, compared to 5 quietly breathing controls under anaesthesia). Typical features of arousal were selected in 101 patients with SDB divided to 5 groups of severity.

Results: The most severe SDB (apnoea hypopnoea index 58.5 ± 2.1/h, M ± SE) had lower (p < 0.05, by t-test) minimum and average O2 saturation (59.7 ± 2.6% and 86, 6 ± 1.2%), accompanied by higher respiratory (75.8 ± 15, 3/h) and lower non-respiratory arousal (47.4 ± 7.0/h) than the other 4 groups. Significant 1.6-12-fold increase (Mann Whitney test) in the number of many brainstem neurones in respiratory and cardiovascular control mechanisms and in both ascending and descending neurones of RF activated by AR was observed in 14 of 35 nuclei, defined according to Berman’s stereotaxic atlas. Respiratory group neurons showed strong recruitment in Comissural nuclei of NTS (10-times, p < 0.01), Ambigual, Paraambigual and Facial nuclei (12×, p < 0.02), reflecting the powerful spasmodic inspiratory activity of the AR. Also the cardiovascular group neurones showed increased FLI, particularly in Nucl. retrofacialis (10×, p < 0.01), indicating strong cardiovascular effects of the AR, providing various clinico-physiological implications. The neurones of the Reticular activating
system showed also an increased number of FLI dots in the Medullary lateral and Magnocellular tegmental fields (11×, p < 0.02), Pontine lateral and Magnocellular fields (3×, p < 0.02) and Area mesencephalis ventralis -tegmentum Tsai (1.6×, p < 0.05), explaining the powerful arousal and revitalisation effects of the AR. The descending reticular tract neurones were strongly activated, too, particularly in the Raphe nuclei (5×, p < 0.02) and the Paragigantocellular nucleus (2.5×, p < 0.02). Recruitment of many brainstem respiratory, cardiovascular and RF neurones in animal studies predisposes the AR for probable reversal of various paroxysmal dysfunctions (e.g. hiccough, laryngo- or bronchospasm, absence epilepsy, hypoxic coma, autoresuscitation from asphyxia, cardiac dysrhythmias and even ventricular fibrillation or imminent brain death).

Conclusion: Immunohistochemical c-Fos study indicated very strong neuronal activation by AR of the brainstem respiratory and cardiovascular control mechanisms and both the ascending and descending parts of RF in cats. The results suggest that the AR can be a very useful model for studies of various influences on 3 main vital functions and their mutual interaction.
Insomnia

P 001
Sleep-related declarative memory consolidation is impaired in patients with primary insomnia

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Aims: While there is now strong evidence that a central cognitive function of sleep is to consolidate newly acquired memories for long-term storage in healthy sleepers, investigations of sleep-related memory consolidation in patients with sleep disturbances are missing yet. Primary insomnia is a suitable model to investigate the consequences of disturbed sleep on memory consolidation, since this disorder is characterized by an isolated disturbance of sleep that is not associated with other somatic or psychiatric malfunctions. Therefore, it is possible to investigate acute as well as long-term consequences of sleep disturbances on memory consolidation free from interference through other disorders which could influence memory consolidation, e.g., depression. In this study, we investigated whether this memory consolidating function of sleep is impaired in patients with chronic primary insomnia, by probing the hippocampus-dependent declarative memory system and the non-declarative procedural system, which is not hippocampus-dependent.

Methods: Sleep EEG, plasma cortisol concentrations and overnight memory consolidation were compared in sixteen patients with primary insomnia and thirteen healthy controls. Tasks of declarative and non-declarative memory (as a control task) were learned before sleep and retrieval was tested after sleep.

Results: There were no differences between patients and controls in the performance level at learning before sleep. After sleep, patients displayed a distinctly lower retention of declarative memory at retrieval than controls (p < 0.05). This difference was not due to differences in alertness as there were no differences between the groups in an extensive test battery of alertness. Patients had a diminished amount of SWS (p < 0.05). Overnight retention of declarative memory correlated significantly with slow wave sleep (SWS) in the controls (r = .69), but with REM sleep in the patients (r = .56). Higher plasma cortisol levels at the end of the first night-half were associated with impaired retrieval of declarative memory after sleep for both controls (r = -.52) and patients (r = -.46). There was no difference between the groups in the non-declarative control task as expected.

Conclusions: Patients with primary insomnia showed a diminished sleep related consolidation of declarative memory. Higher levels of overnight declarative memory consolidation are associated with high amounts of SWS and low plasma cortisol levels during the early part of the night. REM sleep might have a partly compensatory role in declarative memory consolidation if SWS is decreased.

P 002
Disturbed Sleep: Are there Differences in Subjective Symptom Assessments between RLS Patients and Patients with Primary Insomnia?

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Introduction: Disturbed sleep is the cardinal symptom of insomnia; however, sleep disturbances are also common in patients suffering from neurological disorders like Restless Legs Syndrome (RLS) or psychiatric disorders like depression. Among patients with sleep disturbances, RLS is frequently under-diagnosed. We compared RLS patients to patients with primary insomnia with regard to differences in sleep quality, depressive symptoms, quality of life as well as in RLS-specific measures to identify possible different profiles of subjective symptoms between both groups.

Methods: In a diagnostic study, we interviewed by telephone a cohort of all patients who were presented to our sleep lab for diagnosis of sleep disturbances. Patients were asked to remember the status prior to their first treatment and respond to the following questionnaires: Sleep Questionnaire SF-B (quality of sleep subscale), WHO-5 well-being index, Short-Form 12 quality of life as well as RLS-specific questionnaires on symptom severity (IRLS, RLS-D, JHRLS, RLS-DI).

Results: Of 265 patients in the cohort with sleep disturbances as reason for the diagnostic assessment in the sleep lab, N = 179 (67.2%) participated in the interview (females: 64.8%, mean age: 56 years). N = 86 patients had a final diagnosis of RLS and in n = 69 patients diagnosis was primary insomnia (INS), according to two independent neurologists (inter-rater reliability: kappa = 0.93). Sleep quality was described very poor in both groups (SF-B: RLS: 1.1, INS: 1.2, p = .23 (U-test); RLS-6 item sleep quality: 8.0 vs. 7.9, p = .89). Also, daytime somnolence was equally pronounced in both groups (RLS-6: 6.0 vs. 6.2, p = .73). Depressed feelings were mild (WHO-5: 9.5 vs. 10.4, p = .43) on average. No difference between both groups could be found in the standardized physical (42.1 vs. 44.3, p = .22) and the mental (41.0 vs. 40.2, p = .76) component scale of the SF-12 quality of life questionnaire. On the other
side, marked differences (p < .001 for all variables) were detected between RLS and INS groups in RLS-specific scales: IRLS: 30.1 vs. 2.5, John Hopkins RLS Severity Scale: 2.6 vs. 0.3. Also in the RLS-Diagnostic Index (RLS-DI: 15.9 vs. −10.7), both groups were highly different: As expected, RLS symptoms were more severe in RLS patients in these scales.

Conclusions: There are no striking differences between patients suffering from RLS and INS with regard to subjective quality of sleep, depressed feelings, or quality of life. However, RLS patients can be easily identified by the essential diagnostic criteria for RLS which were absent in almost all of the insomnia patients. We recommend the use of a RLS-specific diagnostic instrument like the RLS-DI in all patients who are affected by sleep disturbances to confirm or exclude a diagnosis of RLS.

P 003
Acute Administration of Gaboxadol Improves Sleep Initiation and Maintenance in Patients with Primary Insomnia

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Aims: Gaboxadol is a selective extrasynaptic GABA agonist in development for the treatment of sleep disorders. This study was designed to evaluate its acute efficacy and safety in the treatment of primary insomnia (PI).

Methods: This was a randomised, double-blind, 3-way crossover, polysomnograph (PSG) study designed to compare 5 mg and 15 mg doses of gaboxadol to placebo (PBO) in 26 PI patients aged 18–65 years. Patients met the DSM-IV criteria for PI and the following PSG criteria: latency to persistent sleep (LPS) < 420 min and wakefulness during sleep (WDS) > 48 min or > 10 night awakenings (NAW). Gaboxadol or PBO was administered 30 min before bedtime on two nights during 3 periods separated by 7-14 days. The patients’ own evaluation of their sleep was recorded using the Leeds Sleep Evaluation Questionnaire. Next day residual effects were evaluated using the Cognitive Drug Research test battery.

Results: The per protocol efficacy analyses (n = 23) were based on pooled data from nights 1 and 2 and are presented as means. Both gaboxadol doses significantly improved TST (5 mg: 419.8 min, 15 mg: 420.3 min, PBO: 408.7 min) and reduced total time awake (5 mg: 58.2 min, 15 mg: 57.3 min, PBO: 68.5 min) with no effect on WDS or NAW (although both doses significantly reduced WDS on night 1). Only 15 mg significantly reduced LPS (23.6 min vs PBO: 30.0 min). Slow wave sleep (SWS) was significantly enhanced by 15 mg only (113.5 min vs PBO: 93.9 min).

Patient reports of reduced time to sleep and increased sleep quality showed significant improvement. No next day residual effects were observed. All adverse events were mild or moderate.

Conclusion: Acute administration of 15mg gaboxadol improved sleep initiation and sleep maintenance as well as enhanced SWS in patients with PI. Objective improvements were complemented by subjectively reported improvements in sleep quality and latency. Gaboxadol was well tolerated with no next day residual effects.

This research was supported by H. Lundbeck A/S.

P 004
Family studies in insomnia

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Aims: Several predisposing factors to insomnia have been hypothesized, including a familial component; however, few studies have focused on this topic. The aim of this study is to evaluate the prevalence of insomnia among first-degree relatives of chronic insomniacs and to compare the symptoms between sporadic and familial insomnia.

Methods: Two hundred fifty-six consecutive chronic insomniacs completed a clinical interview, psychometric questionnaires, a questionnaire on the family history of insomnia and, when indicated, a polysomnography. A control group was performed to estimate a base-rate incidence of insomnia in their families.

Results: Patients with primary (n = 75) and psychiatric (n = 100) insomnia were definitely included. Of those with primary insomnia, 70.1% reported familial insomnia compared with 20.4% in the noninsomnia control group. Among the psychiatric insomniacs, 39.8% reported familial insomnia. The mother was the relative most frequently affected. Comparisons between the family prevalence rates of insomnia assessed by the probands and by first-degree relatives show high concordance. A tendency to a younger age at onset was observed in familial and primary insomnia.

Conclusion: This study reports a significant increase of familial aggregation of insomnia, warranting further genetic studies in primary insomnia with early age at onset.

P 005
Insomnia in cancer populations: Preliminary exploration of the relationship between insomnia and cancer-related quality of life

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Insomnia is common in cancer patients. Kaye et al. found that 45% of cancer patients had insomnia compared with 14% of controls. In 1998, Tjemsland et al. reported one-third of breast cancer patients continuing to have difficulty falling asleep 1 year after surgery, compared to half at 6 week, and in 2001, Savard et al. reported that 43% of women with breast cancer had insomnia symptoms and 21% met diagnostic criteria for chronic insomnia. In 1986, the World Health Organisation stated sleep improvement as one of its primary aims in cancer relief efforts. This priority was later reflected by the finding that sleep problems were ranked the fifth highest of 14 distressing symptoms before cancer treatment and the fourth highest after treatment.

**Aim:** To explore the relationship between cancer-related quality of life and insomnia across a range of cancer types.

**Methods:** This report summarises data drawn from an ongoing RCT of psychological treatment for insomnia in cancer patients. Participants from 4 cancer groups (breast, prostate, colorectal and gynaecological) who satisfied diagnostic criteria for persistent insomnia completed baseline sleep assessments along with a range of rating measures indexing disease specific quality of life. These data were first analysed descriptively, and then correlational methods were applied to investigate the association between sleep and QoL.

**Results:** Of the first 133 participants (44M/89F, mean age=61yrs) randomised into the trial, 78 (58.6%) had breast cancer, 31 (23.3%) had prostate cancer, 22 (16.5%) had colorectal cancer and 2 (1.6%) had gynaecological cancer. Preliminary descriptive analyses of baseline sleep variables (i.e. Pittsburgh Sleep Quality Index (PSQI), Dysfunctional Beliefs and Attitudes Scale (DBAS-10) and Sleep Diary) were calculated. The Sleep Diary data show mean (SD) scores of 13.31 (2.87) (PSQI) and 82.58 mins (64.34) (WASO), 384.14 mins (105.87) (TST) and 74.43% (18.32) (SE). The rating scale data indicate mean (SD) scores of 13.31 (2.87) (PSQI) and 5.20 (1.66) (DBAS-10). Correlational analyses were conducted on these clinically relevant sleep variables and on cancer-related QoL measures. These analyses indicated several significant relationships involving small to moderate correlation between (i) physical QoL (PQoL) and PSQI scores (r=0.22, p=0.04), (ii) PQoL and DBAS-10 scores (r=0.30, p=0.004), (iii) emotional QoL (E-QoL) and DBAS-10 scores (r=0.22, p=0.035), (iv) functional QoL (FQoL) and PSQI scores (r=0.34, p=0.001) and (v) FQoL and DBAS-10 scores (r=0.26, p=0.015).

**Conclusions:** These data indicate the existence of a significant relationship between physical, emotional and functional cancer-related quality of life variables and clinically relevant sleep variables.

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trend for CSF CRH to increase with aging was found only in controls (r = 0.3; P < 0.09); patients did not show a significant association here. Finally, CSF neuropeptide concentration at baseline did not differ between the group of elderly patients with insomnia and healthy controls.

Conclusions: Our study corroborates the evolving concept that zolpidem effect various components of the HPA system with the net result of a reduction in its activity. In addition, we found CSF CRH and CSF somatostatin concentrations to be better reflections of age than of insomnia and, finally, that during aging and during insomnia the HPA system changes in similar directions.

P 008
The pharmacokinetic properties of gaboxadol, a new hypnotic, in young and elderly men
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Introduction: Gaboxadol is a selective extrasynaptic GABA agonist in development for the treatment of insomnia. An extensive pharmacokinetic and tolerability study was performed. This abstract presents results from young and elderly men.

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

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

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

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

P 009
Periodic limb movements in patients with insomnia, anxiety and depression
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Aims: chronic insomnia is very common in the general population and psychiatric disorders are diagnosed in about 80% of the cases. Some studies have shown that chronic insomnia increases the risk for development of major depressive episodes. If sleep disease is considered as a cause for mental impairment, we could expect increased prevalence of primary sleep disorders in mentally ill patients and this was not confirmed in the literature.

Methods: we analyzed the data from 40 patients with chronic insomnia, anxiety and depression. In all patients history of insomnia (The Pittsburgh Sleep Quality Index = PSQI), co-morbid diseases, intake of medicaments and demographical data, were recorded. Also standard overnight polysomnography (PSG) using CATEEM (Computer Aided Topographical Electroencephalometry, MediSyst GmbH, Germany) system was performed in all patients. Sleep analysis included following parameters: sleep efficacy, sleep onset latency, total sleep time, percentage of sleep stages and maximal power in beta1, beta2 and delta EEG frequency bands. All polysomnographies were checked manually in order to find out the existence of periodic limb movements during sleep (PLMS).

Results: 40 patients with a mean age 47 ± 14 years (24 women and 16 men) were included in the study. Mean sleep stage percentages in the whole group were as follows: sleep stage 1- 17% ± 11%, sleep stage 2- 18% ± 8%, sleep stage 3- 17% ± 11%, sleep stage 4- 5% ± 5%, REM- 10% ± 3%, movements- 8% ± 4%, wake- 24% ± 15%. The mean sleep efficacy was 65% ± 14%. The following co-morbid sleep diseases were find out: PLMS in 15 patients (37.5%), sleep apnea in 3 patients (7.5%), sleep disordered breathing during REM sleep in 12 patients (30%), combined pathology (sleep apnea and PLMS) in 2 patients (5%), sleep state misperception in 4 patients (10%). PSQI was best determined by anxiety severity (r = 0.008) and the presence of higher maximal power in the beta2-frequency band during sleep (r = 0.008). In the PLMS group statistically higher age, prevalence of male pole, decreased sleep efficacy and increased level of anxiety were found.

Conclusion: We find out a higher prevalence of some co-morbid primary sleep disorders in our patients with
insomnia and mental diseases. The high prevalence of PLMS has great importance from a practical point of view. PSG should more often be performed in patients with chronic insomnia and mental complaints in order to set the appropriate diagnosis.

P 010
Prevalence and Correlates of Nonrestorative Sleep Complaints in those 65 years and Older
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Introduction: Difficulty initiating sleep (DIS) and difficulty maintaining sleep (DMS) are two commonly analyzed subjective sleep complaints. Most studies have focused on these two symptoms and next day consequences when looking at the prevalence and correlates of insomnia. Nonrestorative sleep (NRS) is also a primary insomnia symptom as described in the DSM-IV; however, few studies have looked at this symptom. This study assesses the prevalence and correlates of NRS in an elderly population compared to those with only DIS or DMS.

Methods: Data on over 14,000 elderly (≥65 years) men and women from the baseline assessment of the “Established Populations for Epidemiologic Studies of the Elderly” conducted by the National Institute of Aging were used to examine the prevalence of NRS and associated risk factors. Cases were defined using the EPESE baseline survey instrument which asks one question about the frequency of DIS, two questions about DMS, and one question about NRS (feeling rested on awakening in the morning). Subjects that responded “most of the time” to the DIS or either DMS question and/or “rarely or never” to the NRS question were selected as cases for analysis. The EPESE surveys were conducted on the entire study population in East Boston and Iowa and on a randomly stratified- and area- sample in New Haven and Duke respectively. Weights for each stage of the sample were used to produce unbiased point estimates for variables of interest. The procedure uses the Taylor expansion method to estimate sampling errors of estimators based on the complex sample designs.

Results: NRS was reported by 12.9% (95% CI, 12.1%-13.8%) of this elderly population. More women than men reported NRS (13.9% vs. 11.3%). Of these individuals with NRS, 29.9% rated their health status as 'Poor, Very Poor, or Bad' versus only 5.9% that rated their health status as 'Excellent'. NRS patients were also found to be more likely to smoke (19.7%) and have depressive symptoms (29.1%) relative to those with only difficulty initiating sleep (4.2% smoke; 5.6% depressive symptoms) or difficulty maintaining sleep (15.9% smoke; 16.7% depressive symptoms).

Conclusion: This is one of the first studies to analyze the prevalence and correlates on NRS. As defined above, NRS affects more than 1 in 10 individuals. NRS is associated with lower self reported health status and higher reported depressive symptoms.

P 011
Daytime heart rate variability, blood pressure variability and baroreceptor sensitivity in patients with primary insomnia compared to healthy controls
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Introduction: Insomnia presents as one of the most common sleep disorders in western industrialized countries. Prevalence rates between 5% and 10% are found in the adult population. Due to non-restorative sleep, insomnia reduces daytime functioning as well as quality of life. A state hyperarousability is associated with insomnia at night. Consequently, autonomous tone is modulated. As it is not known whether autonomous alterations persist during daytime we evaluated these and compared to a group of healthy controls.

Methods: To asses the effects of isolated insomnia we excluded secondary insomniacs. Diagnosis of primary insomnia was made using DSM-IV criteria. Psycho-pathology and sleep characteristics were assessed using standardized interviews and questionnaires (MINI/BDI/PSQI/ESS). Blood tests, ecg and urin drug screening were performed. Respiratory related sleep disorders as well as periodic leg movement disorder were excluded using an Embletta polygraphic screening device. The healthy sleepers control group excluded sleep pathology by polysomnography. Measurement of heart rate variability (HRV), blood pressure variability (BPV) and baroreceptor sensitivity (BRS) by ecg and noninvasive portapres technology took place between 9 and 12 am following a standardized protocol. Patients and healthy sleepers were matched for age and gender. Variance analysis for different respiration frequencies as well as Mann-Whitney-U-Test for analysis of group differences within only one frequency were calculated using SPSS-software.

Results: Analysis of preliminary data of 10 primary insomniacs compared with data of 10 healthy sleepers showed no significant difference for HRV, BPV and BRS during daytime.

Discussion: Taking into account the reduced number of patients in this preliminary analysis, we will have to underline these results with more data. However, the available data suggests that no significant effect of primary insomnia on observed parameters of daytime autonomous tone will be found.
P 012
Monitoring of the sleep environment-an evolutionary hypothesis of insomnia

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Mammalian sleep and its complex architecture represent biological adaptations that are highly preserved during evolution. However, many details remain poorly understood, including the ultradian rhythm of NREM and REM cycles. According to a hypothesis of Voss [Rev Neurosci 15:33–46] the frequent shifts between sleep phases with low and high arousal thresholds allow a periodic screening of the sleep environment for danger signals. It has been previously shown that in humans, subjects with opposing information processing styles, monitors and bluters, are differently susceptible to sleep disturbance. So far, no data exist on monitoring and blunting in patients with insomnia. We have investigated insomnia patients who underwent polysomnography in a sleep laboratory with the Monitorer Blunter Questionnaire. We assessed the association between monitoring and physiological sleep parameters as well as the intervening influence of personality. Results will be discussed in the context of evolutionary hypotheses of sleep.

P 013
Sleep Training: a brief, effective intervention to treat insomnia with or without comorbid psychiatric disorders

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Aims: Insomnia is a very common disorder affecting 15–30% of the normal adult population. Much higher is the degree of people suffering from insomnia in a psychiatric inpatient population due to the higher percentage of patients with comorbid psychiatric illnesses i.e. depression, anxiety or personality disorders. Nonpharmacological interventions like cognitive behavioral therapy are well known to be effective in the treatment of insomnia, but the intervention requires normally an out patient setting and involves 6 to 10 distinct sessions. This is not easily applicable in inpatients because of time restriction. Moreover, isolated treatment of insomnia by cognitive behavioral therapy in patients with psychiatric comorbidities is thought to be rather ineffective. We developed a short intervention program called Sleep Training, involving two sessions of group therapy, which was offered to insomniaics during hospitalisation in a general psychiatric clinic. Sleep Training mainly provides information about sleep and sleep hygiene in order to reduce stress-induced hyperarousal states, and sleep restriction to increase sleep pressure.

Methods: We included 40 patients (29 females and 11 males, mean age 47 years) with chronic insomnia according to ICD-10 criteria. All of the patients were hospitalised in a psychiatric clinic and most of them suffered from an additional psychiatric disorder. Excluded were only patients with severe depression or manic or psychotic symptoms. All patients were assessed with a standardized questionnaire on quality of sleep prior to the first session, at the second session and 3 months after Sleep Training.

Results: After only one session of Sleep Training we observed a significant improvement of sleep quality and an improvement of other factors that usually go with insomnia like daytime sleepiness and concentration deficits. All in all, an increased satisfaction of the individuals could be noted. The improvement of symptoms remained stable after 3 months.

Conclusions: Our study demonstrates that Sleep Training is an effective method to treat insomnia in an inpatient setting and a stable improvement of symptoms can be obtained. Furthermore, Sleep Training is also helpful for patients with psychiatric comorbidity-an important finding if one looks at the fact that insomnia related to a psychiatric disorder often results in a chronic sleep problem. Finally, Sleep Training is very economic and less time-consuming than other forms of therapy as e.g. cognitive behavioral therapy.

P 014
Longterm effects of a multicomponent sleep restriction therapy with initial inpatient treatment for psychological insomnia

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Introduction: Sleep restriction therapy with inpatient treatment (ISSRT, Initial Stationäre Schlafrestriktionstherapie) is a multicomponent method for patients with psychophysiological insomnia. The first week of this modified sleep restriction is inpatient intervention, the following 7-week therapy period is outpatient. The core of ISSRT is sleep restriction completed by sleep hygiene education, individual meetings, different cognitive methods, photo therapy and relaxation techniques.

Method: 48 Patients participated in the study. They all had complained about physiological insomnia and took part in the 8-week-therapy program between April 2002 and April 2004. Patients who suffered from other sleep
disturbances as sleep apnea, RLS or PLMS were excluded, as well as Patients with mood disorders. Patients reported their sleep quality, sleep efficiency, total sleep time, wake after sleep onset and the sleep onset latency in sleep diaries and additionally different questionnaires (PSQL, BDI, FEPS I & II, ESS) were assessed. The Data was assessed pre and post treatment (Post1) and again twelve weeks (Post 2) and one year (Post 3) after the therapy. T-tests for dependent samples were performed on reported data prior to the treatment and to the data at the different post treatments.

Results: Sleep Latency decreased sharply from 89 minutes before to 44 minutes after treatment and reduced further to 31 (Post 2) and 27 (Post3). The total sleep time increased from a baseline of 251 to 348 minutes after treatment and remained stable (344 Post 2 and 351 Post 3). The gain of the total sleep time led to an increase of sleep efficiency. From a pre-treatment 55%, sleep efficiency raised to 84% after twelve weeks and to 81% at the one year follow up. The PSQI-Score showed an reduction from 14.1 before treatment to 8.5 after three month.

Discussion: The follow up data showed that the short term effects of the ISSRRT remained stable after one year. An initial inpatient phase in the course of sleep restriction therapy seems to be an promising approach for insomniacs who shown no improvements in outpatient intervention.

Narcolepsy

P 015
Impaired glucose tolerance in patients with narcolepsy
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Aims: Recent studies have focused on the interaction between sleep regulation and metabolism, owing to the important role of the orexin-neuropeptide system in sleep regulation and pathophysiology of narcolepsy and due to its involvement in the regulation of body weight. To address this issue we performed glucose tolerance tests in narcoleptic patients and healthy controls.

Methods: We have examined 9 patients with narcolepsy and cataplexy (7 males and 2 females; mean age 34.4 ± 10.8 years; mean BMI 25.8 ± 3.2 kg/m²) and 9 healthy controls matched for sex, age and BMI. Venous blood glucose and insulin levels, glycated hemoglobin (HbA1c), plasma-cortisol, -ACTH, -cholesterol, -triglyceride and -leptin levels were assessed. At 0800h the subjects were offered either a 75 g/300 ml glucose or a similar sorbitol sweetened drink, followed by drawing blood samples for glucose at 0, 30, 60, 120, 180, 240 min.

Results: Four of the 9 narcoleptic patients (44.4%) but no healthy subjects had a 120 minutes blood glucose level above 140mg/dl indicating a pathological glucose tolerance. The AUC for the glucose condition was significantly higher in patients suffering from narcolepsy than in healthy controls (28248.3 vs. 25676.7 min mg/dl; t[8]=2.662; p=0.029; effects size d=0.80). The percentage of HbA1c was found to be significant higher in narcoleptic patients than in controls (5.41% vs. 5.01%, t[8]=2.353; p=0.049; effects size d=0.71), however the other metabolic and endocrine parameters did not differ between both groups.

Conclusions: The glucose tolerance in narcoleptic patients is impaired. HbA1c shows a slight but significant increase in that group. Disturbed glucose metabolism might be a genuine feature of narcolepsy.

P 016
Delay in diagnosis of narcolepsy is associated with poorer quality of life
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Aim: Narcolepsy is a chronic and little known sleep disorder characterised by excessive daytime sleepiness, cataplexy, sleep paralysis and hallucinations. Its prevalence is about 0.03–0.05%. Our research hypothesis was that a delay in diagnosis of narcolepsy is associated with decreasing quality of life.

Methods: Data were collected from a Norwegian cohort representing 180 persons with narcolepsy. A questionnaire (SF-36) was sent to all of them. The response rate was 78%. We considered patients with associated cataplexy. The delay of diagnosis was estimated as the difference between age of diagnosis and age at symptoms debut. We considered Spearman Correlation Coefficient to estimate the association between delay in diagnosis and quality of life parameters using SF-36.

Results: There were adverse associations between Social functioning and delay r = −0.25 (p<0.01), Physical functioning and delay r = −0.23 (p<0.02) and Role physical and delay r = −0.22 (p<0.02). There was also an association between Bodily pain and delay r = 0.28 (p < 0.004). There was no sign. association between General health and delay, neither with Vitality, Role emotional or Mental health.

Conclusions: Delay in diagnosis is associated with increased social and physical problems for people with narcolepsy. Identifying narcolepsy (with treatment and support) soon after disease onset may prevent medical, occupational and social complications.
P 017
Postoperative outcome of patients with narcolepsy

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Aims: To determine the postoperative outcome of narcolepsy patients, a population that may be at increased risk of perioperative complications, including postoperative hypersomnia, prolonged emergence after general anesthesia, and apnea.

Methods: The perioperative outcome of pharmacologically treated narcolepsy patients, was studied. A total of 30 narcolepsy patients was identified. Charts were reviewed for the following perioperative (intraoperative time plus recovery room time) events: time for extubation, duration of stay in the Postnaesthesiology Department, and duration of stay in the hospital. Furthermore, any of the following complications were noted: electrocardiographic (ECG) changes, postoperative nausea and vomiting, hypotension, subjective reports of pain, decreasing oxygen saturation (SpO2) levels, respiratory complications, postoperative fever, agitation in the Postnaesthesiology Department, and hypersomnia in Postnaesthesiology Department. In addition, patient hospital stay and major morbidity and mortality during hospital stay were recorded.

Results: Ten patients pharmacologically treated for their narcolepsy symptoms that underwent 24 noncardiac surgical procedures under general anesthesia. We found no evidence that the pharmacologically treated narcolepsy patients were at any increased risk for perioperative complications. Furthermore, their time for endotracheal extubation, length of stay in the Postnaesthesiology Department and hospital did not differ from nonnarcolepsy patients.

Conclusion: Pharmacological therapy for narcolepsy should be continued during the perioperative period. In addition, treated narcolepsy patients are at no increased risk for postoperative complications.

P 018
A 12-week Randomized, Double-Blind, Placebo-Controlled Study of Armodafinil in Adults with Excessive Sleepiness Associated With Narcolepsy

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Aim: In patients experiencing excessive sleepiness associated with narcolepsy, there are some patients for whom the wake-promoting effects of modafinil, when given once daily, wear off in the afternoon. This study evaluated the efficacy and safety of armodafinil, the longer acting enantiomer of modafinil, in patients who experience excessive sleepiness associated with narcolepsy.

Methods: Patients with ICSD diagnosis of narcolepsy, mean sleep latency (MSL) on Multiple Sleep Latency Tests (MSLT) <6 minutes, and CGI-S >4 were enrolled in this 12-week randomized, double-blind, placebo-controlled trial. Patients received armodafinil 150 mg, armodafinil 250 mg, or placebo once daily. The Maintenance of Wakefulness Test (MWT) was performed at 2-hour intervals at weeks 4, 8, and 12 and last post-baseline visit. Clinical Global Impression of Change (CGI-C), ESS, Brief Fatigue Inventory (BFI), and tests of cognitive function from the Cognitive Drug Research System (an instrument that can be used to detect alterations in the efficiency of cognitive functioning) were also assessed. MWT (mean sleep latency of first 4 naps) and CGI-C were primary measures (combined doses vs placebo). Safety assessments included adverse events and nighttime polysomnography.

Results: 326 patients were screened; 196 were randomized (placebo, n=64; armodafinil 150 mg/day, n=65; armodafinil 250 mg/day, n=67). Seventy-three percent of patients were Caucasian; 56% were female. The average age of patients was 38.1 years (range 18-67). Patients treated with armodafinil demonstrated a significant improvement from baseline MSL (4 daytime trial average) on the MWT (p <0.01) and percentage of patients who improved on the CGI-C (p <0.0001) relative to placebo. Improvements were seen in quality of episodic memory (p <0.05) and power of attention (p <0.05); ESS (p <0.01); and global fatigue from the BFI (p =0.01). MSL and power of attention were also improved later in the day (p =0.04 and p =0.04, respectively). All improvements on clinical efficacy measures were achieved early in the day and were maintained throughout the day. Armodafinil was generally well tolerated, with no adverse effect on nighttime sleep. Only headache appeared to be dose-related.

Conclusions: Armodafinil significantly improved wakefulness in patients with excessive sleepiness associated with narcolepsy. Wakefulness was sustained throughout the day. Significant improvements were also seen in memory, attention, and fatigue. Armodafinil was generally well tolerated with no adverse effect on nighttime sleep.

P 019
Driving licence regulations for narcolepsy in European Community

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Aim: Narcolepsy is a serious chronic disease. There are evidences that narcolepatic patients have a higher risk for driving accidents, even if with an inter-subject variatbility for driving performance. The European Community (EC) discipline of “Minimum standards of physical and mental fitness for driving a power-driven vehicle”, from the Annex III to the Directive of the Council 91/439/EEC of 29 July 1991, classified drivers in Group 1 and Group 2 (i.e. drivers of heavy vehicles). Annex III to EC Directive provides driving licence restrictions for generic “sudden disturbances of the state of consciousness”, other than epileptic disorders, without to mention any specific criteria for narcolepsy. The aim of this study is to investigate the existence of national regulations for driving licence release to people suffering for narcolepsy in the EC Countries before the 2004 enlargement (the Fifteen).

Methods: We performed a survey, trying to obtain information from the authorities of the Ministry of Transport of the Fifteen by phone or e-mail. The answers were classified in the following two categories: (1) Countries which apply only Annex III to EC Directives; (2) Countries with specific regulations for narcolepsy.

Results: We obtained answers from all but Be and Fr; about the latter, information were found in the world wide web. Eight Countries apply only Annex III to EC Directive, while within the seven remaining this discipline has been improved by specific regulations where, in principle, symptomatic patients are considered unfit to drive. Narcolepsy-specific regulations are different for Group 1 and 2 but for ES, where driving licence is in general denied, except under direct medical responsibility and with a restricted period of validity. Group 1 licence regulation provide that driving licence is (1) releasable only after a free symptoms period of one year (Nl) or six months (Be), with a restricted validity (five yrs Ni, two yrs Be); (2) releasable only to treatments-responder patients (Fi, Fr, Sw, UK), with a restricted period of validity (one-three yrs UK, under medical judgement Fi, Fr and Sw). Group 2 licence regulation provide that driving licence is: (1) releasable only after a free symptoms period of five years with a restricted validity (five yrs) in Ni; (2) in general denied but for symptoms-free patients (with different definitions) on individual basis judgement (Fr, Sw and UK); 3) always denied in Be and Fi.

Conclusions: Eight out of Fifteen EC Countries do not provide specific regulations for driving licence release to patients with narcolepsy. In the remaining Countries, regulations for fitness of patients affected by narcolepsy show a wide-spread variation not only about the criteria for licence release but also about its period of validity. Moreover, there is not any reference to objective methods used to evaluate the pathology (i.e. scale or laboratory exams) and improvements after the treatment.

P 020
HLA-DQB1*0602 and CSF-hypocretin in Danish Narcolepsy Patients

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Based on data from USA, Central Europe, Korea and Japan, Narcolepsy-Cataplexy (NC) has been found to be highly associated (90-100%) with HLA-DQB1*0602 and abnormally low levels of CSF-hypocretin (<110 pg/ml) across ethnic groups. Narcolepsy without clear-cut cataplexy (narcolepsy with atypical cataplexy (NaC) and narcolepsy without cataplexy (NwC)) is also associated with HLA-DQB1*0602 (40-56%) as compared to the general population (12-38%), and although rare, low CSF-hypocretin can be found in narcolepsy without clearcut cataplexy. The existence of HLA-DQB1*0602-negative narcolepsy patients and patients with normal CSF-hypocretin levels, makes it clear that HLA-typing and measurement of CSF-hypocretin cannot function as isolated tools in diagnosing narcolepsy, but both parameters has found their use as standards of comparison between studied narcolepsy populations.

Aims: No data has ever been published about Danish narcolepsy patients. We therefore wanted to investigate if the Danish population of narcolepsy patients also has association to HLA-DQB1*0602 and abnormally low levels of CSF-hypocretin, and thereby is comparable to other studied populations.

Methods: Patients were diagnosed according to the International Classification of Sleep Disorders (and the suggested expansion of the criteria for NwC: sleep latency ≤8 minutes and ≥2 SOREMPs on MSLT). Eleven Danish narcolepsy patients, all Caucasian (5 clear-cut NC, 2 narcolepsy with atypical cataplexy, 4 NwC) were diagnosed via clinical interview, PSG and MSLT at Center for Sleep Disorders, Glostrup University Hospital, Denmark. Blood sample for HLA typing and lumbar puncture for measurements of CSF-hypocretin (RIA, Phoenix Inc.) was performed in all diagnosed patients willing to participate.

Results: All 5 patients with clear-cut NC were DQB1*0602 positive (2 homozygote, 3 heterozygote) and had abnormally low levels of CSF-hypocretin (13–50 pg/ml). In the non-clear-cut cataplexy group, all 6 patients had normal levels of CSF-hypocretin (232–558 pg/ml), 1 NwC was DQB1*0602 positive (heterozygote) and the rest (2 NaC, 3 NwC) were HLA-DQB1*0602-negative.

Conclusions: The association of HLA-DQB1*0602 and abnormally low levels of CSF-hypocretin is also a characteristic of Danish NC patients. The Danish NC population is therefore comparable to other studied NC populations. Danish narcolepsy patients without clearcut cataplexy also have normal levels of CSF-hypocretin,
confirming that low CSF-hypocretin is generally not a characteristic of this group of patients. However, Danish narcolepsy patients without clear-cut cataplexy do not seem to have the previously described higher association to HLA-DQB1*0602 than the general Caucasian population, though one must consider the limitations of the small sample of patients. The association of HLA-DQB1*0602 and CSF-hypocretin levels is currently being studied in a larger population of Danish narcolepsy patients.

P 021
N-REM-sleep alterations in narcolepsy/cataplexy

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Aims: The NREM sleep patterns of adult and young adult narcoleptic patients with cataplexy were studied focusing not only on the conventional sleep parameters but also on sleep “microstructure” analyzing the cyclic alternating pattern (CAP).

Methods: Forty-nine HLA DQB1*0602-positive patients with narcolepsy/cataplexy (32 men and 17 women, aged 18–46 years) were included in the study together with 37 age-matched normal controls. Each subject underwent one polysomnographic night recording after an adaptation night. Sleep stages were scored following standard criteria and each CAP A phase was detected in each recording, during NREM sleep and classified into three subtypes (A1, A2, and A3). Various CAP parameters were computed and used for statistical analysis. The same channel used for the detection of CAP A phases was divided into two-second mini-epochs which were assigned to a sleep stage and to a CAP condition. Power spectra were calculated from each mini-epoch for frequencies between 0.5 and 25 Hz with a frequency step of 0.5 Hz. Average spectra were obtained for each CAP condition, separately in sleep stage 2 and SWS, for each subject.

Results: Narcoleptic patients displayed significantly reduced total CAP rate, because of its reduction during sleep stage 2 and SWS. The percentage of A1 subtypes was reduced and A2 and A3 subtypes were increased. This disproportion was due to a selective significant reduction in the number of A1 subtypes/hour and, to a lesser extent, to a reduced A3 index. Finally, a significant difference was also found for the average number of CAP sequences which was smaller in narcoleptic patients than in controls. The comparison between the EEG sleep power spectra showed that narcoleptic patients had significantly higher power spectra for fast frequencies (17.0–17.5 to 25.0 Hz) in NREM sleep stage 2 and SWS, while REM sleep power spectra showed significantly higher power density for frequency bins 0.5–1.5 Hz, 7–12.5, and 13.5–25 Hz. Similarly, CAP A1 subtypes and NCAP epochs during sleep stage 2 and SWS displayed significantly higher power density for fast frequency bins.

Conclusions: The new finding of our study is that NREM sleep is altered in narcoleptic patients; NREM sleep microstructure, as reflected by CAP and the corresponding EEG spectral analysis, was significantly impaired. The neurophysiological alterations of NREM sleep in narcolepsy might also influence the important cognitive processes which are believed to take place during this sleep stage.

P 022
Predictors of health-related quality of life in patients with narcolepsy

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Aims: No prospective survey investigated the clinical course of narcolepsy. Health-related quality of life (HRQoL), measured by the 36-Item Short Form (SF-36), was demonstrated to be a valid prognostic measure in sleep disorders. Cross-section designed studies disclosed that two clinical factors (excessive daytime sleepiness (EDS) directly, and the disease duration inversely) determine an impairment of SF-36 scales in narcolepsy. To disclose the evolution of HRQoL of patients with narcolepsy and the role of the state of mood as influencing factor, we performed a five-year prospective cohort study.

Methods: Fifty-four adults with narcolepsy (mean age 49 years; 77% men) from the sleep center of the Department of Neurological Sciences of Bologna, self-administered the SF-36 and the Zung’s depression scale in 1999 and 2004.

Results: Sex and age standardized score of role functioning-physical (RP), general health (GH), vitality (VT), social functioning (SF), role functioning-emotional (RE) and mental health (MH) were lower than the Italian norm in the observations of 1999 and 2004 (RP from −0.78 to −0.70, GH from −0.33 to −0.32, VT from −0.62 to −0.64, AS from −0.82 to −0.76, RE from −0.71 to −0.60, MH to −0.33 to −0.40). By means of multiple linear regression some of the variance of these scores (R-square from 0.35 to 0.67) were explained by EDS, measured by Epworth sleepiness scale (inverse correlation), state of mood (inverse correlation), disease duration (direct correlation).

Conclusions: This prognostic study, to our knowledge the first with a prospective design in narcolepsy, disclosed
that (1) RP, VT, SF and RE were the most impaired scales in patients with narcolepsy; (2) the HRQoL profile was stable across five years of evolution of the disease; (3) together with EDS and disease duration the mood state of patients seems to play a relevant role in influencing HRQoL. These findings strongly suggest the need for additional cognitive and behavioral therapies in narcolepsy.

P 023
Immunologic Analisys in Narcolepsy—Cataplexy

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Aims: Narcolepsy has been associated with HLA DQB1*0602 allele along with decreased hypocretin CSF levels. Autoimmune process has been suggested as a possible etiology. The aim of this study was to quantify the total lymphocyte count and its subpopulations in narcoleptic patients with cataplexy.

Methods: A total of 22 patients with narcolepsy from the outpatient clinic of Instituto do Sono were selected. Peripheral blood draw was performed in narcoleptic patients and 23 healthy controls. Lymphocytes counts were performed using flow cytometry and immunofluorescence staining. Lymphocytes subpopulations were distinguished using specific cell surface markers. Data were compared between groups using Student t-test (p < 0.05).

Results: Narcoleptic patients were 12 men, aged 19 to 65 years. Six narcoleptic subjects had frequent cataplectic attacks. Healthy subjects were 14 men, aged 20 to 65 years. The total lymphocyte count, CD4 T-cell, CD8 T-cell and CD19 B-cell were not different between narcoleptics and controls. Nonetheless, patients with frequent cataplexy had significant lower CD19 B-cell (248 ± 123 vs 379 ± 130) than patients with rare or absent attacks (p = 0.041).

Conclusion: These data suggest a depletion of CD19 B-cells in patients with severe manifestation of narcolepsy-cataplexy.

Support: AFIP & FAPESP-CEPID

P 024
Identifying brain target regions of modafinil in narcolepsy by low-resolution brain electromagnetic tomography (LORETA) and psychometric correlation analyses

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Introduction: Vigilance promotion of modafinil was demonstrated as early as in 1986 by our pharmaco-EEG studies in normal elderly subjects and later by clinical trials in narcolepsy. Recently, utilizing low-resolution brain electromagnetic tomography (LORETA) we showed a functional deterioration of the fronto-temporo-parietal network of the right-hemispheric vigilance system in narcolepsy and a therapeutic effect of modafinil in the left hemisphere, which is less affected by the disease. The aim of this study was to investigate whether vigilance changes at the neurophysiological level correlate with cognitive or thymopsychic alterations at the behavioral level.

Methods: EEG-LORETA and psychometric data were obtained in 15 narcoleptics before and after 3 weeks of placebo or 400 mg modafinil daily. Noopsychic investigations included the Pauli Test and complex reaction time, thymopsychic measures the BF-Wellbeing Score, the Beck Depression Score, the State-Trait Anxiety Inventory and the VAS of drive, mood, affectivity and wakefulness. Critical flicker frequency (CFF) was evaluated, too.

Results: In psychometry, cognitive performance (Pauli Test) was significantly better after modafinil than after placebo. There were no significant differences in reaction time, CFF or thymopsychic variables. At the neurophysiological level, LORETA demonstrated an improvement of vigilance, characterized by an increase in fast alpha-2 power in the fronto-temporal and sub-lobar cortical regions of the left hemisphere, a beta-1-3 power increase in many brain regions, predominantly in the left hemispheric temporo-parietal and limbic cortices, a delta and theta power decrease in frontal lobes, a theta power increase in the temporo-parietal region of the left hemisphere and a delta power increase in the left parietal cortex and in the right more than the left occipital and limbic lobes. Correlation analyses revealed that a decrease in prefrontal delta-theta and alpha-1 LORETA power and in alpha anteriorization correlated with an improvement in cognitive performance. Moreover, a positive correlation was found between drowsiness and theta power in parietal and medial prefrontal regions and beta-1 and beta-2 power in occipital regions.

Discussion: The modafinil-induced improvement of vigilance objectified by electrophysiological neuroimaging in various brain regions correlated with an improvement of cognitive performance and daytime sleepiness at the behavioral level.

P 025
Simultaneous Occurrence of Narcolepsy and Sleep-Disordered Breathing

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Aims: Given the prevalence of sleep disordered breathing (SDB) and the increased rates of obesity among narcoleptic patients narcolepsy and SDB can occur simultaneously.

Introduction: Sleep disordered breathing (SDB) and narcolepsy are frequent sleep disorders. The presence of SDB is a risk factor for the development of narcolepsy, and vice versa. In a study of 151 patients with narcolepsy, 23% had obstructive sleep apnea syndrome (OSA). In a study of 69 patients with SDB, 23% had cataplexy. The aim of this study was to investigate the simultaneous occurrence of narcolepsy and sleep disordered breathing in a sample of 871 patients with SDB.
However, there is only limited data in the literature about clinical importance.

Methods: Retrospective characterization of all patients with the diagnosis of narcolepsy who were admitted to our sleep laboratory since 2003.

Results: 15 patients were diagnosed with narcolepsy according to standard criteria (9 male, 6 female, mean age 36, range 9–80 years, BMI 28 ± 6.6 kg/m², ESS 16 ± 3, mean sleep latency on MSLT 6 ± 3.1 min). In 7 patients SDB was also found (RDI 18 ± 9/h, mostly OSA). Narcoleptic patients with SDB tended to be older (43 ± 20 vs. 30 ± 18 years) than those without. For these patients the time from initial sleep evaluation to diagnosis of narcolepsy also appeared to be longer (2.9 ± 4 vs. 0.6 ± 2 years). Of these patients, 4 benefited long term from CPAP therapy, one patient did not tolerate CPAP. In 2 patients therapy of the SDB was not felt to be necessary. Contrary to the literature we did not find increased rates of central events.

Conclusions: Among patients with narcolepsy diagnosed in a sleep laboratory associated with a department of respiratory medicine up to half of the patients were found to simultaneously have SDB.

Respiratory Sleep Disorders

P 026
Effect of obesity and severe obesity on sleep related breathing disorders before and during CPAP therapy

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Aims: There is growing evidence that obesity—even in the absence of sleep related breathing disorders (SRBD) affects negatively the sleep, possibly due to metabolic or circadian disturbance. The aim of this study was to compare the sleep quality in non-obese, obese and severely obese patients with SRBD, before and after normalisation of breathing with CPAP therapy.

Methods: The sleep parameters were compared retrospectively between 18 non-obese (Body Mass Index-BMI <25.7) and 18 obese (BMI 30 to 40) and 17 severely obese (BMI > 40) patients with obstructive SRBD (ICSD 780.53-0; all groups age and gender matched with mean age 55.2 ± 9.7, 55.6 ± 9.5 and 55.5 ± 9.4 respectively.) We compared the polysomnographic recordings before CPAP (baseline), at the second night under CPAP (CPAP-engagement) and three months after CPAP-engagement (CPAP-control). The sleep parameters were scored according to standard criteria. For statistic the Mann-Whitney-Test was used.

Results: At baseline the respiratory parameters of severely obese and obese group differed from the non-obese group. (Apnea Hypopnea Index-AHI: 82.3 ± 23.6 p < 0.01; 66.9 ± 21.6 p < 0.01; 29.5 ± 18.7 resp.) During CPAP-engagement only severely obese group differed from non-obese (AHI: 2.0 ± 3.1 p < 0.03; 1.5 ± 2.1 p = 0.2; 0.8 ± 1.7). There was no differences at CPAP-control (AHI: 1.3 ± 2.4 p = 0.78; 1.3 ± 1.9 p = 0.29; 0.7 ± 1.0). At baseline, sleep parameters of the severely obese group showed lower percentage (of total sleep time) of REM, S2 and S4, and a higher percentage of S1 than the non-obese patients (4.7 ± 5.2 vs. 8.3 ± 4.2 p < 0.02; 26.5 ± 10.9 vs. 35.5 ± 8.9 p < 0.03; 3.5 ± 6.0 vs. 8.1 ± 6.6 p < 0.01; 33.2 ± 16.4 vs. 19.2 ± 9.5 p < 0.01). During CPAP-engagement the REM percentage of severely obeses became higher and the S1 and S2 lower than of non-obeses (21.6 ± 7.0 vs. 11.8 ± 4.0 p < 0.01; 7.8 ± 3.8 vs. 13.3 ± 6.7 p < 0.01; 24.3 ± 7.9 vs. 31.1 ± 9.5 p < 0.04). There was no differences between both groups at CPAP-control. The obese group revealed at baseline higher S1 percentage than the non-obese group (29.7 ± 13.3 vs. 19.2 ± 9.5 p < 0.01). During CPAP-engagement obese patients showed higher percentage of REM (15.8 ± 7.0 vs. 11.8 ± 4.0 p < 0.05) and at CPAP-control higher percentage of S3 than non-obese patients (12.8 ± 4.4 vs. 9.5 ± 3.2 p < 0.03).

Conclusions: Our data suggest there is no significant effect of obesity and severe obesity on sleep in SRBD, under long term CPAP therapy. The differences in sleep parameters during CPAP-engagement suggest more pronounced sleep-rebound in obese and severely obese patients with SRBD. The results obtained at baseline confirmed previously known association between obesity and severity of SRBD.

P 027
Elevating the head of the bed during sleep reduces snoring

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Aims: No longer recognized as a mere nuisance, snoring is a primary sleep disturbance which carries health risks for diabetes and cardiovascular disease. We tested the hypothesis that snoring could be ameliorated by adaptively elevating the head of a segmented bed.

Methods: This is an ongoing study of 15 subjects (median:range age 53 years; 23:75; weight 90 kg; 66:115) with moderate/severe snoring using laboratory polysomnography and a bed whose “head” (80 cm long) could be smoothly raised to a maximum angle of 32° under remote control. Though initially supine, the head was raised in 5° increments after each 5 minute period of persistent snoring. If snoring ceased for 15 minutes, the bed was then incrementally lowered. Statistical analyses contrasted the incidence of snoring between 8 minute periods
immediately-preceding and -following each elevation using a GEE regression model (R-language, 2.0).

Results: Elevating the head of the bed after persistent snoring reduced the incidence of snoring an average of 70% (Odds ratio = 0.3, 95% CI = -0.2:0.7, robust z = -5.5, p = -0). EEG micro-arousals accompanied 28% of the bed adjustments (n = 177) without wake.

Conclusions: While studies of non-surgical snoring aids (e.g., lubricants, nasal-strip, pillows) have generally not been confirmatory, our adaptive bed control was effective and is favored over fixed elevation for comfort and to minimize orthostatic cardiovascular loading. A fully automated system is now undergoing trials.

**P 028**

**Association of obesity to autonomic neuropathy highly increased the occurrence of obstructive sleep apnea in diabetic subjects**

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Previously we reported that 30% of non obese diabetic subjects affected by autonomic neuropathy (DAN) have sleep obstructive sleep apnea/hypopnea. The underlying mechanism could be related to an impairment of the upper airway reflexes, possibly due to the alterations of the nerves fibers involved in their regulation. The aim of this study was to establish if the addition of an anatomical factor, as the fat periharyngeal apposition in obesity, to a functional damage, could increase the occurrence of obstructive sleep apnea (OSA) in diabetic subjects suffering from autonomic neuropathy. At this purpose, 10 obese diabetic subjects without autonomic neuropathy (ObDAN-), age 56 ± 2.5 years, BMI 37 ± 1.5 Kg/m², neck circumference-NC 46 ± 1.3 cm, DAN score 1 ± 0.2), 7 obese diabetic subjects with autonomic neuropathy (ObDAN+, age 55 ± 3.0 years, BMI 35 ± 1.8 Kg/m², NC 47 ± 1.0 cm, DAN score 6.4 ± 0.8) and 10 obese non diabetic subjects (Ob, BMI 34 ± 4.0 Kg/m², NC 45 ± 6.0 cm) underwent to cardio-respiratory polysomnographic study in the sleep laboratory. All ObDAN+, 3 ObDAN- and 4 Ob have AHI > 20; all ObDAN+, 2 ObDAN- and 4 Ob have and AI > 10. The mean lowest O₂ saturation (MLO₂Sat) was less than 90% in all ObDAN+, in 3 Ob DAN- and in 4 Ob. Considering only OSA subjects, the percent of the index time spent with HbO₂Sat less than 90% was 22, 5 and 9 in ObDAN+, ObDAN- and Ob, respectively. These data suggest that the association of obesity to autonomic diabetic neuropathy increased the number of events, the severity of HbO₂ desaturations and the time of hypoxia during sleep. These factors add a further risk factor to a disease with an increased cerebro and cardiovascular morbidity and mortality, per see

**P 029**

**Treatment of sleep disordered breathing with the automated nCPAP device “Delphinus” (Viasys)-Comparison with conventional nCPAP therapy**

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Aims: The aim of the study was to investigate whether the automated nCPAP device “Delphinus” is as effective as conventional manual nCPAP in the treatment of sleep disordered breathing in an unselected patient group, titrated on nCPAP for the first time. We defined therapeutic equivalence of both treatment modalities as the Apnea-Hypopnea-Index (AHI) using “Delphinus” being not more than 2.5 events/h higher than using conventional nCPAP.

Methods: We performed a standard polysomnography as baseline measurement. In case of sleep disordered breathing that had to be treated, we also performed standard polysomnography during both titration nights. Since we expected systematic differences between the first and the second titration night, we balanced the sequence of treatment modalities. Testing of equivalence was performed by means of the t-test for equivalence.

Results: We investigated 40 patients (4 drop-outs because of technical problems, 36 analysed, 30 men, 6 women).

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</table>

Figure 1

The AHI under treatment using “Delphinus” automated nCPAP and the AHI under treatment using conventional nCPAP turned out to be equivalent using the fore mentioned criterion. Furthermore, there were no relevant clinical differences within the nCPAP pressure, the sleep stage distribution and sleep efficiency (SE) between both treatment modalities.

Conclusion: Despite some technical difficulties (4 drop-outs) and some sizable differences between both treatment modalities in few patients we found therapeutic equivalence compared to manual nCPAP-titration. This study was supported by Viasys Healthcare.
P 030
Comparison between the Rad-9 pulse oximeter with Masimo SET technology and the Nellcor NPB 290 pulse oximeter

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Aims: Continuous measurement of arterial oxygen saturation and peripheral pulse (pulse oximetry) is an established standard procedure in sleep medicine. However, most devices used at present have problems concerning the accuracy of measurement due to movement artefacts or because of minor perfusion. There are study results, showing higher reliability of the Masimo device in experimentally induced “critical” conditions (such as movement artefacts or diminished perfusion) compared to other pulse oximeters. Up to now, no studies were performed, showing these positive effects during routine examinations in the sleep lab.

Methods: We performed polysomnographic examinations with the SIDAS-GS-System (Heinen und Löwenstein GmbH). All study recordings were scored by one experienced sleep technician. None of the recorded oxygen saturation signals were shown within the scoring procedure. Scoring of sleep disordered breathing (SDB) was exclusively done with the following signals: Airflow (nasal/oral) with thermistor Thoracic and abdominal movements (induction plethysmography) Snoring (Microphone) Heart Rate

Results: We investigated 20 patients (15 men, 5 women).

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</table>

Figure 1

All oxygen saturation values below 40% were scored as artifacts. Artifact time also included the time the patient was disconnected because of nycturia or other reasons. The artefact time of both devices did not differ significantly (Masimo: 56.2 ±110.7 sec., Nellcor: 107.7 ± 193.49 sec.). The Masimo device showed significantly lower mean saturation values (95.31 ±2.2%) compared to the Nellcor device (96.82% ± 1.96%). On average Masimo detected more desaturations than the Nellcor device, however these differences were not significant (205.95 ±140.74 vs. 197.05 ±140.11). Using the Masimo device, 53.04% of all detected desaturations were associated with respiratory events. The Nellcor device had 50.11% of the desaturations matched with respiratory events.

Summary: Although this pilot study only showed statistically significant differences in the mean saturation, it is worthwhile noting that all analysed parameters of the Masimo device differed in the expected, positively rated, direction from those of the Nellcor device. However, the dimension of these differences is only marginal, so they might not have any influence in clinical routine.

This study was sponsored by Heinen & Löwenstein.

P 031
Continuous positive airway pressure therapy in patients with overlap syndrome

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Background: Continuous positive airway pressure (CPAP) is the treatment of choice for patients with obstructive sleep apnea (OSA). The effects of CPAP therapy in patients with chronic obstruction pulmonary disease (COPD) in association with OSA (overlap syndrome) have been still controversial.

Purpose: The aim of this study was to investigate the efficiency of CPAP therapy in patients with overlap syndrome.

Patients and Methods: Results of treatment were studied in 32 patients with overlap syndrome (males, average age 48.36 ± 8.64, mean body mass index BMI 33.2 ± 5.1). We evaluated the results of CPAP therapy by the levels of apnea-hypopnea index (AHI) and the mean oxygen saturation during sleep (SaO2). All patients were investigated for 2-3 nights by overnight polysomnography (PSG) (Embla, Island). Titration of CPAP with the purpose of establishing the minimal effective pressure level was made manually under the control of PSG.

Results: The AHI reduced significantly to normal values in all the patients, 25% (8) of patients still had nocturnal hypoxemia (SaO2 was less then 89%). These patients demand nocturnal oxygen therapy.

Conclusion: CPAP therapy is effective in patients with overlap syndrome. Nevertheless, the CPAP therapy has to be controlled by the oxygen saturation level in order to be combined, when necessary, with nocturnal oxygen therapy for the effective management of overlap syndrome.

P 032
Anthropometric, clinical, functional data in prediction of obstructive sleep apnea

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Purpose: This study was initiated to evaluate the connection between anthropometric, clinical, lung
functional features and severity of obstructive sleep apnea (OSA), represented by apnea-hypopnea index (AHI).

Patients and Methods: We studied clinical data, including the baseline dyspnoea index (BDI), excessive daytime sleepiness, wake up arterial hypertension, anthropometric parameters (body mass index (BMI), waist-to-hip ratio (W/H), neck circumference), pulmonary function tests, hematological results, blood gases in 360 obese male patients with OSA, confirmed by overnight polysomnography (Embla, Island), without chronic airflow obstruction. A stepwise multiple regression analysis was performed attempting to predict the value of AHI.

Results: The level AHI was influenced significantly by the mean level of vital capacity, BID, W/H, the level of red blood cells, the presence of excessive daytime sleepiness and wake up arterial hypertension ($R^2 = 0.886; p = 0.00051$). No relations were detected between AHI and BMI, neck circumference

Conclusion: In most patients we observed a strong relationship between OSA severity and anthropometric, clinical, functional data resulted in cardiorespiratory abnormalities and abdominal type of obesity. In prospective studies a regression model, using these variables, may be of use for the prediction of OSA.

P 033
Five years experience of somnological centre in St.Petersburg.
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Between 2000–2005 1134 patients were referred to our somnological centre for assessments. In 542 (47.79%) subjects (82% male, 18% women) diagnosis of obstructive sleep apnea (OSA), including mild OSA (194–35.79%), moderate (111–20.48%), severe (236–43.52%), was confirmed by overnight polysomnography (Embla, Island). In most patients we observed a strong relationship between OSA severity and anthropometric, clinical, functional data resulted in cardiorespiratory abnormalities and abdominal type of obesity. The most common diseases accompanying OSA were obesity (86.2%), hypertension (81.1%). 206 (38%) patients were treated by diet therapy, 119(21.96%)-by upper airway surgery including soft-tissue remodeling, 86(15.86%) were undergoing long-term treatment by continuous positive airway pressure.

P 034
Dyspnoea in patients with obstructive sleep apnea
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Background: Sleep-disordered breathing is often associated with the high risk of cardiorespiratory diseases (CRD). Dyspnoea is the most important symptom in CRD.

Purpose: The aim of this study was to evaluate clinical characteristics of dyspnoea on the basis of the relatively homogeneous study population with obstructive sleep apnea (OSA).

Patients and Methods: We analyzed clinical characteristics, including the Baseline Dyspnoea Index (BDI), 6 minute walk test (6-MWT), pulmonary function in 360 obese male patients with OSA, confirmed by overnight polysomnography (PSG) (Embla, Island), without chronic airflow obstruction and chronic heart failure.

Results: 183 (50.83%) patients reported excessive daytime sleepiness, 100% patients reported different severity of dyspnoea. Patients with more severe dyspnoea were heavier, and had more severe OSA in PSG testing. BDI was highly correlated to apnea-hypopnea index (AHI) ($r = -0.60; p < 0.005$), nocturnal desaturation ($r = -0.45; p < 0.005$). The mean oxygen saturation during sleep ($SaO_2$) ($r = 0.43; p < 0.005$). 6-MWT was highly correlated to BMI ($r = -0.62; p < 0.005$), AHI ($r = -0.57; p < 0.005$). Stepwise multiple regression analysis revealed that the BDI was influenced significantly by the mean level of $SaO_2$, AHI and BMI ($R^2 = 0.46; p < 0.0001$).

Conclusion: Dyspnoea is a common symptom in patients with OSA. The mechanisms of dyspnoea include sleep-disordered breathing (by nocturnal desaturation and sleep hypoxemia) and obesity, associated with reduced physical work capacity. We consider OSA as an independent risk factor in determination of chronic respiratory failure.

P 035
Association of Serotonin Transporter Gene Polymorphism with Obstructive Sleep Apnea Syndrome
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¹Gazi University, Faculty of Medicine, Department of Pulmonary Disease, ²Department of Otorhinolaryngology, ³Mersin University Department of Medical Biology and Genetic

Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive pharyngeal collapse during sleep. There is genetic predisposition to sleep disorders. Synaptic 5-HT is inactivated by presynaptic reuptake, which is mediated by the serotonin transporter. Blockage the serotonin transporter leads to increased extracellular 5-HT. Polymorphism of the serotonin transporter gene (STG) leads to alterations in serotonin level, and may be
important in OSAS. We aimed to assess the role of STG polymorphism in OSAS. Twenty-seven OSAS patients and 162 healthy volunteers were involved in the study. STG polymorphism was investigated using leucocytes obtained from peripheral blood. There was no difference between the genotypes and allele frequencies of the patients and controls regarding VNTR and HTTLPR polymorphisms. VNTR and HTTLPR variants and the frequencies of 12/12, 12/10, L and S alleles were not significantly different between male and female controls (MC, FC). 12/12 and SS genotypes were overrepresented in the female patients (FP) while 12/10 and LL genotypes were overrepresented in the male patients (MP). Genotypes 12-12 were overrepresented in the MC while the genotypes 12-10 and L/S were overrepresented in the MP. Alleles 10 and L were more frequent in the MP than MC. Genotypes of FP and FC were not significantly different. Allele 10 and L were less frequent in the FP than FC. STG polymorphism seems associated with the occurrence of OSAS, especially in MP. Absence of association between genetic variants and polysomnography findings may suggest that some mechanisms other than STG polymorphism are involved in OSAS pathophysiology.

P 036
The Role of smoking habits on Obstructive Sleep Apnea

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Univ Fed Sao Paulo, Psychobiology Dept, Brazil

Introduction: It‘ is known that smoking impairs lung function and that smokers present a high frequency of sleep complaints. However, the association between smoking habits and obstructive sleep apnea (OSA) is still controversial.

Aims: To clarify the role of smoking as a risk factor for OSA.

Methods: A randomized sample of 950 cases with basal oxyhemoglobin saturation (SaO2) over 90% and with no treatment for OSA was selected from the database of the Sleep Institute of Sao Paulo. Anthropometric characteristics, smoking habits, apnea and hypopnea index (AHI) and total sleep time with SaO2 < 90% (TST with SaO2<90) were compared between pack-years categories (p-ys): 0 (non smoker), < 15, 15–30, ≥ 30. Regression analyzes was performed to evaluate the p-ys categories as a risk factor to AHI categories (<5, 5–15, 15–30, ≥30) and to TST with SaO2<90 categories (<5%, ≥5%), before and after adjusted for anthropometrical variables without correlation to p-ys.

Results: Table 1: Patients characteristics according to p-ys

<table>
<thead>
<tr>
<th>Pack-years categories</th>
<th>0</th>
<th>&lt;15</th>
<th>15–30</th>
<th>&gt;30</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>583</td>
<td>153</td>
<td>98</td>
<td>116</td>
<td></td>
</tr>
<tr>
<td>Age (SD)</td>
<td>44.7 (13.7)</td>
<td>40.6 (12.5)</td>
<td>49.3 (11.4)</td>
<td>53.9 (9.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (SD)</td>
<td>28.4 (5.4)*</td>
<td>28.7 (5.7)</td>
<td>29.0 (5.1)</td>
<td>30.0 (4.6)*</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>66.0%</td>
<td>69.9%</td>
<td>71.4%</td>
<td>77.6%</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>34.0%</td>
<td>30.1%</td>
<td>28.6%</td>
<td>22.4%</td>
<td></td>
</tr>
<tr>
<td>Smoking habits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>non</td>
<td>100%</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>current</td>
<td>0</td>
<td>50.3%</td>
<td>43.9%</td>
<td>31.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>former</td>
<td>0</td>
<td>49.7%</td>
<td>56.1%</td>
<td>69.0%</td>
<td></td>
</tr>
<tr>
<td>AHI (SD)</td>
<td>20.8 (24.0)</td>
<td>22.9 (24.8)</td>
<td>25.5 (25.0)</td>
<td>25.4 (24.1)</td>
<td></td>
</tr>
<tr>
<td>TST with SaO2&lt;90 (SD)</td>
<td>12.7 (25.9)</td>
<td>13.0 (26.1)</td>
<td>18.2</td>
<td>23.5</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

There was a positive correlation between p-ys and age (r=0.5, p<0.001), so the parameter age was not included on further analyzes. On logistic regression analyzes, p-ys was not a risk factor for the AHI categories over 5. In comparison to non smoker, the risk of having ≥5% TST with SaO2<90 is 1.7 times higher to 15–30 p-ys (95%CI = 1.1–2.7, p=0.01) and 3 times higher to ≥30 p-ys (95%CI = 1.9–4.6, p<0.001). After adjusting for BMI and gender, the category 15–30 p-ys (OR = 1.7, 95%CI = 1.1–2.7, p=0.03) and ≥30 p-ys (OR = 2.5, 95%CI = 1.6–3.9, p<0.001) were still a risk factor to have ≥5% TST with SaO2<90.

Conclusion: P-ys wasn‘ t a significant risk factor for the diagnosis of OSA, however it was a significant risk factor for TST with SaO2<90 ≥5%, even after adjusting for other confounding variables.

Smokers with higher number of p-ys are older and more former smoker compared to smokers with low number of p-ys.

Support: AFIP, FAPESP/CEPID

P 037
The role of esophageal pressure measurement for the detection of the CPAP-pressure in patients with obstructive sleep apnea syndrome

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Introduction: Adjustment of sufficient nasal CPAP-therapy in patients with OSAS can be time-consuming and so a parameter, which can predict the adequate pressure would be desirable. The goal of our study was to find out if the esophageal pressure as a measure of the breathing effort during polysomnography is helpful for the prediction of the effective CPAP-pressure.
Methods: 20 patients with OSAS received diagnostic polysomnography with measurement of the esophageal pressure during the whole night. After introduction of nasal CPAP-therapy the connection between esophageal pressure and the effective nCPAP-pressure was examined.

Results: Mean nCPAP-pressure was 8.6 (± 2.4) mbar with an pretherapeutic apnea-hypopnea-index (AHI) of 44.7 (± 15.7). There was a poor correlation between the mean esophageal pressure (7200–9800 breaths per patient) on the one hand and the effective nCPAP-pressure on the other hand (Spearman correlation: r = 0.42; p < 0.05). This was similar to the poor correlation of the nCPAP-pressure and the AHI (r = 0.48; p < 0.05). A better correlation was seen between the maximum esophageal pressure and the nCPAP-pressure with r = 0.57 (p < 0.01). The best correlation in this small subgroup was seen between the body mass index and the nCPAP-pressure with r = 0.82 (p < 0.01). This correlation was not found in a larger collective. There was no influence of age of the patients to the required nCPAP-pressure.

Conclusion: Polysomnographic parameters as for example the AHI and the mean esophageal pressure are only of limited value for the prediction of the effective nCPAP-pressure in patients with OSAS. Maximum esophageal pressure perhaps in combination with other anatomical factors may be helpful for enclosing a certain pressure area.

P 038 
Cardiac Troponin I Levels and Relationship with Cardiovascular Morbidity in Patients with Obstructive Sleep Apnea Syndrome

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As a result of repeated nocturnal hypoxemia, pulmonary arterial vasoconstriction, acute right ventricular dilatation and hypokinesis and at the end, myocardial injury may occur in patients with obstructive sleep apnea syndrome (OSAS). As it is known, cardiac troponin I is an important predictor of myocardial injury. The aim of this study is to investigate the degree of myocardial injury which is created with nocturnal hypoxemia by measuring cardiac troponin I levels in patients with OSAS. 76 subjects were examined with polysomnography and classified according to their apnea-hypopnea index (AHI). 47 patients with AHI > 5 were considered as OSAS and 29 subjects with AHI < 5 were included into control group. OSAS patients were divided into three groups according to their AHI values as mild (AHI = 5–15), moderate (AHI = 15–30) and severe (AHI > 30) OSAS. Serum troponin I levels were measured in all subjects. When the levels of troponin I were compared, there was no significant difference between patients and controls (OSAS = 3.64 ± 2.7 and controls = 3.13 ± 1.83, p = 0.18). Also no significant difference were detected between mild (2.49 ± 0.93), moderate OSAS (2 ± 0.51) and controls comparing with their troponin I levels (p = 0.79 and 0.56, respectively). But levels of troponin I in patients with severe OSAS (3.47 ± 1.83) were significantly higher than controls (p = 0.01). There was a significant positive correlation between AHI and troponin I levels in patients with OSAS, (r = 0.38, p = 0.01). In conclusion, this study has been thought that cardiac troponin I measurements may be useful to show the degree of myocardial injury in severe OSAS.

P 039 
Nocturia and Enuresis Associated with Obstructive Sleep Apnea

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Obstructive Sleep Apnea Syndrome (OSAS) is commonly associated with obesity, loud snoring and daytime sleepiness. Nocturia is a less frequent and less well recognized finding and enuresis has been rarely reported as a complication of OSAS. We report a series of six patients (4 male, 2 female, ages 25-64, avg 37.7) with OSAS, nocturia and enuresis. All the patients were obese (BMI 34 to 56, avg 41.7), complained of snoring and were excessively somnolent during the day. Enuresis occurred occasionally in 2 and nightly in 4 patients. The duration of enuresis prior to evaluation ranged from 5 months to 26 years.

Polysomnography was performed on all patients in an accredited Sleep Disorders Center. In 5 patients moderate to loud snoring and severe OSAS (RDI 75-139, avg. 114; all with desaturations below 79%) were documented. In one patient only mild snoring and modest OSAS (RDI 9, desaturations to 86%) was noted. All six patients were treated with nasal continuous positive airway pressure (CPAP, range 6–13 cm/H2O, avg. 8.7) and had complete resolution of the enuresis with improvement of snoring and daytime somnolence.

This report is remarkable for the inclusion of 2 women with OSAS and enuresis, which to the best of our knowledge, has not been previously reported. It is also interesting that a mild case of OSAS can be associated with nightly enuresis. All patients had complete and lasting resolution of enuresis with nasal CPAP treatment. Our recommendation is for polysomnography in any patients with unexplained enuresis. Aggressive treatment of OSAS (even mild cases) with nasal CPAP in these patients is recommended.
P 040
Nocturnal Oxygen Desaturation and Charles Bonnet Syndrome

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Background: The Charles Bonnet Syndrome (CBS) is a syndrome of visual hallucinations and fully retained insight in elderly patients with visual impairment. Etiology of the CBS is unclear and drug treatment is rarely successful. As one case report found an association between CBS and nocturnal oxygen desaturations (OD), we investigated the relationship between CBS and OD in elderly patients with visual impairment.

Methods: Patients of an acute geriatric unit with impaired vision (<5%) and without dementia (DSM-IV) were included. Patients with visual hallucinations and retained insight were classified as CBS patients. All patients were studied with computerised nocturnal oximetry.

Results: 107 patients (28% male, 72% female; mean age 83 ± 8y) were evaluated. 17 patients were classified as CBS patients. There was no difference between CBS patients and non-CBS patients in age, sex or medication. The number of oxygen desaturation events per hour recording time (oxygen desaturation index, ODI) was 18 ± 18/h in non-CBS patients and 28 ± 19/h in CBS patients (p < 0.02).

Conclusion: We found an independent and significant association between SDB and CBS. As drug treatment is not effective in these patients, all CBS-patients should be evaluated for SDB. Further research is needed to show whether treatment of SDB will improve CBS.

P 041
Sleep Disordered Breathing and Functional Impairment in Elderly Patients

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Department of Geriatric Medicine, Prosper-Hospital, Recklinghausen, Germany

Background: We objectively evaluated elderly patients to determine the prevalence of sleep disordered breathing (SDB) and whether SDB was associated with functional status and functional outcome.

Methods: Patients admitted for acute deterioration of health status were randomly studied with computerized overnight oximetry for arterial desaturations events, defined as a desaturation of at least 4%. The oxygen desaturation index (ODI) was calculated as the number of desaturations per hour. Patients were observed by staff for evidence of excessive daytime sleepiness (EDS). Functional abilities were measured with the use of the Bathel Index (BI, 0–100) at the time of admission and discharge.

Results: 481 patients (30% male, 70% female; age 81 ± 8y) admitted for neurological diseases including stroke (41%), heart failure (30%), osteoarthritis (12%), pulmonary diseases (12%) or gastroenteral diseases (8%) were included. The 25th, 50th and 75th percentiles of ODI were 4/h, 11/h and 26/h. Data are shown in the table below.

<table>
<thead>
<tr>
<th>ODI (quartiles)</th>
<th>n/h</th>
<th>4–11</th>
<th>11–26</th>
<th>&gt; 26</th>
</tr>
</thead>
<tbody>
<tr>
<td>number of pts.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BI on admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BI on discharge</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDS (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>114</td>
<td>117</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td></td>
<td>56 ± 32</td>
<td>56 ± 31</td>
<td>50 ± 31</td>
<td>44 ± 31*</td>
</tr>
<tr>
<td></td>
<td>69 ± 31</td>
<td>67 ± 21</td>
<td>65 ± 28</td>
<td>56 ± 31*</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>38</td>
<td>31</td>
<td>51*</td>
</tr>
</tbody>
</table>

SDB was associated with lower BI at admission and discharge and with EDS. No associations were found between BI, age, sex or disease admitted for.

Conclusion: SDB is frequent in elderly patients admitted to a geriatric unit. There is an independent association between SDB and low functional status on admission and discharge. SDB is also associated with EDS in elderly patients. Further research is needed to determine whether SDB can be successfully treated in these patients and whether functional outcome will be influenced by treatment of SDB.

P 042
Carbohydrate and lipid metabolism disorders in patients with metabolic syndrome and obstructive sleep apnea

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Background: Obstructive sleep apnea (OSA) is a wide spread disease among obese patients. Obese patients prone to have such a pathological condition as metabolic syndrome (MS). Both play the important role in cardiovascular diseases.

Design and Methods: We have compared the levels of total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride (TG), and glucose during the oral glucose tolerance test (OGTT), and ambulatory blood pressure (BP) monitoring (Spacelabs 90207, USA) in 20 patients with MS and OSA (the index of apnea-hypopnea (IAH)-35,1 ± 23,0) and 8 patients with MS without OSA (IAH 3,4 ± 1,5). All patients underwent night polysomnography (Embla Flaga, Australia). The participants were matched for body mass index, waist/hip ratio and mean BP. All patients had the same hypotensive therapy: ACE inhibitors, β-blockers, calcium channel blockers,
**Results:** The total cholesterol (6.2 ± 1.3 mmol/l versus 6.3 ± 0.8 mmol/l, accordingly, p = n.s); LDL cholesterol (3.8 ± 1.1 mmol/l versus 3.8 ± 0.4 mmol/l, accordingly, p = n.s); HDL cholesterol (1.3 ± 0.3 mmol/l versus 1.4 ± 0.3 mmol/l, accordingly, p = n.s); TG (2. 7 ± 1.6 mmol/l versus 2.2 ± 1.2, accordingly, p = n.s); OGTT (9.1 ± 1.3 mmol/l versus 6.8 ± 1.7 mmol/l, p = 0.005).

**Conclusion:** Patients with MS in association with OSA have significantly higher glucose levels during OGTT than patients with MS only. Parameters of lipid metabolism did not differ in both groups, but there was a tendency to increase of TG in MS and OSA group.

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**P 043**

**Comparison between automatic and a novel fixed positive airway pressure therapy studying quality of life and sleep architecture in Obstructive Sleep Apnea**

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**Introduction:** Quality of life and sleep architecture on CPAP therapy may be influenced by therapy perception. C-Flex technology is supposed to improve patient comfort, therefore we designed a study to compare 2 modes of ventilation, AutoCPAP (REMstar® Auto, Respironics) vs. fixed CPAP with C-Flex (REMstar® Pro with C-Flex™, Resprionic) to evaluate this assessment.

**Methods:** Patients with known Obstructive Sleep Apnea syndrome (AHI ≥ 30/h and Epworth score > 10) were included prospectively in one centre. After 14 days (V1) of auto titration (REMstar Auto), the patients were randomised to Group A: fixed CPAP with C-Flex (using 90% pressure from auto titration); and Group B: AutoCPAP (4–20 cm H2O). Subjects were evaluated at baseline (V0) and 12 weeks (V2, 10 weeks of therapy) with Epworth Sleepiness Scale (ESS), Functional Outcome of Sleep Questionnaire (FOSQ) and full polysomnography on therapy.

**Results:** We report data on 41 patients (A: 20 B: 21). At V0, the 2 groups were equivalent for age, gender, BMI, AHI, ESS, FOSQ, and sleep parameters. At V2, AHI, ESS and FOSQ were equally improved, but C-Flex did show better results for total sleep time (p < 0.01), sleep efficacy (p < 0.025) and deep sleep (p < 0.05). The other sleep parameters were equivalent with a tendency of better REM sleep with C-Flex (p = 0.054, ns).

**Conclusion:** These data suggest that AutoCPAP and fixed CPAP with C-Flex are equally efficient to reduce AHI and improve quality of life. However, patients are sleeping longer and have a better sleep architecture with C-Flex.

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**P 044**

**Quality of life and Depression in Portuguese OSAS patient**

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**Aim:** Prospective evaluation of quality of life and depression in 136 OSAS and treatment response in a subgroup CPAP compliant.

**Method:** Quality of life and depression was systematically and prospectively investigated in 136 men with snoring and daytime sleepiness or fatigue, after eliminating patients with chronic medical or psychiatric disorders and unstable drug regimen. Evaluation included medical and specialized sleep and psychiatric evaluations, Beck Depression Inventory, Quality of Life SF-36, Inventory Epworth Sleepiness Scale (ESS), Sleep Disorders Questionnaire, and polysomnography were performed. 50 patients had follow-up evaluations after 4 weeks controlled CPAP usage. Parametric and non-parametric statistics, Chi-square and multiple regression analysis were performed, adjusted for age and BMI.

**Results:** 136 men were studied. Mean age 52.5 ± 12.3; BMI, 27.9 ± 5.6; AHI, 49.1 ± 26.8; lowest SaO2, 74.2 ± 12.3; TST, 451.7 ± 81.0; arousal index, 33.2 ± 26.2; BDI, 8.3 ± 6.1; SF-36 subscales GH (57.3 ± 17.2) and VT (53.4 ± 22.5) were the most affected. They were divided according the AHI 30. The more severe group AHI > 30 (n = 89) had higher BMI ( < 0.001); ESS(< 0.001), arousal index (< 0.001), lower lowest SaO2 (< 0.001), with similar BDI, and worse score at RP (0.003) and GH (0.024) SF-36 subscales. For the 50 patients CPAP compliance the treatment improve significantly the BDI ( < 0.0001) and all SF-36 sub-scales.

**Conclusion:** Quality of life sub-scales RP, GH are related to OSA severity, although the same was not seen in depression. Nasal CPAP improve quality of life and minor depressive symptoms.

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**P 045**

**Erectile Dysfunction a under diagnosis male OSAS symptom**

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**Aim:** Prospective evaluation of erectile dysfunction(ED) present longer than 6 months in OSA male 60 years old and younger and treatment response in a subgroup CPAP compliant.

**Method:** 98 male osas were systematic prospective evaluated with medical, sleep, psychiatric and sexologic specialized evaluations; measurement of Epworth Sleepiness Scale (ESS), Beck Depression Inventory (BDI), Sleep Disorders Questionnaire, Quality of Life SF-36 and
polysomnography were performed. Parametric and non-parametric statistics, Chi-square, Fisher Exact Test and Multiple regression analysis were performed.

Results: 98 men, 28 presented ED. Patients with ED had significant higher AHI (60 ± 27.9 vs 45.4 ± 27.3), ESS (17.6 ± 4.1 vs 13.7 ± 4.3) and BMI (11.1 ± 7.5 vs 7.3 ± 5.3) lower lowest SaO2 (68.7 ± 13.6 vs 79.9 ± 10.9) and worse score at PF (63.3 ± 20.5 vs 78.8 ± 20.3), RP (54.3 ± 40.3 vs 77.6 ± 33.7), BP (68.9 ± 22.5 vs 77.9 ± 22.8), GH (51.2 ± 12.9 vs 66.6 ± 17.2), VT (41.4 ± 17.5 vs 57.8 ± 21.0) and SF (68.0 ± 22.8 vs 77.4 ± 22.2). From the 28 subjects with ED, 17 were treated with CPAP. Mean age 48.4 ± 9.2 years, mean BMI 32.3 ± 3.7 kg/m², mean lowest SaO2 63.8 ± 10.4%, mean ESS 18.2 ± 3.8, mean AHI 71.4 ± 26.8 events/hour. CPAP resolves 76% of ED cases. No significant differences according age was found between those with and without ED resolution.

Conclusion: ED is related to OSAS severity. OSA must be recognized in patients with erectile dysfunction, as nasal CPAP can eliminate it in many cases, and improve significantly their quality of life.

P 046
The effects of exercise on pulmonary haemodynamics in patients with pure OSAS

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Aim: The aim of our study was to investigate the effects of mild exercise on pulmonary haemodynamics in patients with pure OSAS. Material: 37 pts (males) with OSAS (mean age 46 ± 8 years, mean BMI = 35 ± 6 kg/m², mean AHI = 62 ± 18, VC 4.8 ± 1 L (98 ± 13%N), FEV1 = 3.7 ± 0.8 L (99 ± 14% N), FEV1/VC 78 ± 6, PaO2 = 71.3 ± 7.4 mmHg, PaCO2 = 39.7 ± 3.4 mmHg, pH = 7.39 ± 0.036 and normal pulmonary arterial pressure (PPA) at rest (mean PPA = <19 mmHg) and during exercise (mean PPA = <30 mmHg).

Methods: Full polysomnography, right heart catheterisation at rest and during exercise (40 Wats/6mins).

Results: All pts presented with: mean PPA at rest 14.5 ± 2.9 mmHg and during exercise 28.5 ± 9.5 mmHg; pulmonary wedge pressure (PW) at rest 5.9 ± 2.5 mmHg, during exercise 12.7 ± 7.1 mmHg; cardiac output (CO) at rest 5.2 ± 1.9 L/min., during exercise 9.5 ± 3.9 L/min.; pulmonary vascular resistance (PVR) at rest 154 ± 65 dyne sec cm⁻⁵ and during exercise 149 ± 83 dyn sec cm⁻⁵. In 21 pts we observed normal PPA at rest and during exercise: 13.4 ± 2.9 mmHg/22.1 ± 5.5 mmHg. Patients presented with: mean age 43 ± 8 years, mean BMI 33 ± 5 kg/m², mean AHI 59 ± 20, VC 5.2 ± 0.9 L, (102 ± 10%N), FEV1 4.2 ± 0.7 L, (106 ± 11%N), FEV1/VC 80 ± 5, PaO2 73.7 ± 6.9 mmHg, PaCO2 39.2 ± 3.4 mmHg, pH 7.39 ± 0.034; PW at rest 5.4 ± 2.5 mmHg, during exercise 9.0 ± 4.7 mmHg; CO at rest 5.2 ± 2.0 L/min. during exercise 7.9 ± 4.0 L/min.; PVR at rest 149 ± 74 dyne sec cm⁻⁵, during exercise 164 ± 96 dyn sec cm⁻⁵. In 16 pts we observed normal PPA at rest and elevated pulmonary artery pressure during exercise: mean PPA et rest 16 ± 2.1 mmHg, during exercise 37 ± 7 mmHg. They presented with: mean age 50 ± 7 years, mean BMI 37 ± 6 kg/m², mean AHI 65 ± 16, VC 4.2 ± 0.8 L, (91 ± 14% N), FEV1 3.1 ± 0.6 L (89 ± 13% N), FEV1/VC 76 ± 5, PaO2 68.3 ± 7.1 mmHg, PaCO2 40.5 ± 3.2 mmHg, pH 7.38 ± 0.039; PW at rest 6.4 ± 2.6 mmHg, during exercise 19.1 ± 5.8 mmHg; CO at rest 5.1 ± 1.8 L/min., during exercise 11.7 ± 2.7 L/min.

Conclusions: We observed statistically significant relationship between age, BMI and spirometric parameters in patients with normal haemodynamics data during exercise and in patients with pulmonary hypertension during exercise. Probably it was an effect of large obesity and hypoventilation (although we did not find statistically significant relationship between PaO2). In both group of pts we observed normal PVR at rest and during exercise.

P 047
Pilotstudy of an Auto-Titration Device (SomnoSet®) based on the Combination of FOT, Flow and Snoring Detection vs. standard CPAP

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Introduction: Auto-CPAP devices are used for titration of therapy pressure in patients with obstructive sleep apnea. We studied the efficacy of an Auto-titration device (SomnoSet®, Fa. Weinmann, Hamburg, Germany) controlled by FOT, flow and snoring detection (APAPFOT, Flow), compared to manual CPAP-titration.

Methods: We studied 47 Patients, mean age 55.9 ± 12.6y, mean BMI 33.2 ± 7.1 with OSA (mean ESS 10.2 ± 4.3) treated for first night with the APAPFOT, Flow-titration device, without any modifications of the preset parameters of the device, during full cardiorespiratory polysomnography in the sleep lab. In the second night we performed a manual titration with an identical looking standard CPAP-device (Somnocomfort®).

Results: The mean AHI was reduced from 39.7 ± 19.6 to 7.4 ± 5.5 during APAPFOT, Flow (index for obstructive events 3.7 ± 3.2) and 7.8 ± 7.9 during standard CPAP titration. The arousal index could be reduced from 41.3 ± 20.2 to 6.6 ± 6.4 (APAPFOT, Flow) and 9.2 ± 7.2 (CPAP). The mean time of oxygen saturation lower 90% diminished from 15.9 ± 14.8% to 3.2 ± 7.1% with APAPFOT, Flow and to 3.4 ± 6.55 with conventional
CPAP. The mean APAP pressure was 6.6 ± 2.2 mbar. There was no significant differences in sleep parameters, AHI, Arousal index and Oxygen-Saturation parameters between APAP_FOT,Flow and CPAP night. The mean difference of the effective pressure from the APAP_FOT,Flow night to the effective pressure of the CPAP night was 0.23 ± 2.9mbar. In 17 patients the effective CPAP pressure determined by manual titration was equal to the pressure determined by APAP_FOT,Flow titration. In 16 cases the pressure was higher and in 14 cases lower than the pressure ascertained by APAP_FOT,Flow -titration.

Discussion: In this setting the APAP_FOT,Flow showed reasonable treatment results in patients with OSA. Further studies are required to determine, which pressure of the automatic titration night should be used for a further standard CPAP-therapy.

P 048
First Experiences with an Auto-CPAP-Device (Somnosmart-2®) based on FOT, Flow- and Snoring Detection in Patients with Obstructive Sleep Apnea

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Pneumology, 3rd Medical Department at Klinikum Nuernberg, Nuernberg, Germany

Introduction: Auto-CPAP devices highly depend on their control parameters. Forced oscillation technique (FOT) and flow (volume and “flattening”) are very sensitive non-invasive tools for the assessment of upper airway obstruction during nasal CPAP therapy. We studied the therapeutic efficacy of an Auto-CPAP device (Somnosmart-2®, Fa. Weinmann, Hamburg, Germany) controlled by a combination of FOT, flow and snoring detection (APAP_FOT,Flow).

Methods: We studied 96 patients, mean age 57.4 ± 10.8 yrs. with obstructive sleep apnea (mean ESS 10.2 ± 4.7) treated for first night with the APAP_FOT,Flow during full cardiorespiratory polysomnography in the sleep lab, without any modifications of the preset parameters of the device.

Results: The mean AHI was reduced from 28.5 ± 21.6 to 3.7 ± 3.6 during APAP_FOT,Flow. The index for obstructive events (obstructive apneas and hypopneas) was reduced to 1.8 ± 1.8. The mean time of oxygen saturation lower 90% decreased from 10.6 ± 15.8% to 1.5 ± 5.2%. The arousal index could be reduced from 28.8 ± 20.9 to 4.8 ± 3.4. The mean APAP pressure was 6 ± 1.7 mbar.

Discussion: In this setting, APAP_FOT,Flow (Somnosmart-2®) demonstrated very promising treatment results in patients with OSA, without any individual modifications of treatment parameters. Further studies are needed to determine, whether treatment with APAP_FOT,Flow is more beneficial for the patients than standard CPAP, or treatment with other APAP-devices.

P 049
Long-term quality of life in sleep apnoea

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Sleep apnoea is associated with social consequences, traffic accidents, morbidity and mortality. CPAP is the best documented treatment for moderate-severe sleep apnoea. Short-term studies suggests, that quality of life is improved CPAP, but no studies have evaluated whether chronic long-term treatment has a continuous, lasting positive effect on quality of life.

Methods: 100 consecutive patients evaluated under the clinical suspicion for sleep apnoea during November-December, 2002 were enrolled. All patients were evaluated with basic clinical questionnaire including Epworth Sleepiness Scale and the quality of life questionnaire SF-36 and 15D. Patients with moderate-severe sleep apnoea (AHI exceeding 15 per hour) were treated with auto-adjusted CPAP. June 2004, 1½ year later, all patients were again presented to the questionnaires.

Results: 27 patients and 27 controls (patient who in whom the study were normal or presented only slight sleep apnoea) returned the questionnaire. Patients with sleep apnoea who were treated with CPAP presented significant improvements: (1) In the SF-36 including bodily pain, general health perception and vitality, and (2) in the 15D: quality of sleep, mental function, depression scale, stress, vitality, urinary function and sexual activity. No changes were observed in the control group. Patients who did not present sleep apnoea in the evaluation, presented lower physical scale and bodily pain.

Conclusion: Long-term treatment with CPAP for moderate-severe sleep apnoea improves several domains in quality of life. Patients submitted for sleep apnoea, which do not present sleep apnoea, may have other causes for their sleepiness, which is not identified by PSG.

P 050
Evaluations of daytime sleepiness in male patients with sleep apnoea syndrome


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Aims: Sleep apnoea syndrome is a disorder that causes excessive daytime sleepiness. Excessive daytime sleepiness
causes various types of accident, such as traffic accidents or accidents in nuclear power plants. Therefore, it is important to evaluate daytime sleepiness to prevent these accidents as well as to improve patients’ quality of life. There are several methods to evaluate daytime sleepiness. However, the results of these evaluations are not necessarily unanimous. The present study is performed to clarify the dissociation between evaluations of daytime sleepiness in patients with sleep apnoea syndrome.

Methods: The subjects were 29 male patients with sleep apnoea syndrome. Polysomnography (PSG), Epworth Sleepiness Scale (ESS), Kwanseigaku Sleepiness Scale (KSS), Multiple sleep latency test (MSLT), work performance tests (Uchida-Kreapelin psychodiagnostic test and Bourdon cancellation test) and Minnesota multiphasic personality inventory (MMPI) were performed. ESS and KSS are evaluative scales for subjective sleepiness, while MSLT (neurophysiological) and work performance tests (behavioural) are scales for objective sleepiness. The apnoea/hypopnoea index (AHI) from PSG was used as an indicator of the severity of the disorder because it showed a significant positive correlation with number of stage changes (sleep fragmentation) and time of SpO2 below 90 (hypoxaemia during sleep).

Results: The results of ESS, KSS, MSLT and work performance tests were not correlated with each other. Among these scales for evaluating daytime sleepiness, mean sleep latency (MSL) from MSLT was the only scale that showed a significant correlation with AHI. Other scales were considered to be influenced by various factors, such as patient age or personality traits, which were measured by MMPI.

Conclusions: This results suggested that MSL is the most appropriate scale for evaluating daytime sleepiness caused by this sleep-related breathing disorder.

P 051
Obesity and hypoxia determine the serum levels of leptin and C-reactive protein (CRP) in obstructive sleep apnea patients

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It is well established that serum leptin and CRP levels are increased in patients with obstructive sleep apnea syndrome (OSAS) as well as in obesity. In this study we examined the independent role of obesity in serum levels of leptin and CRP in a cohort of OSAS patients. 76 patients referred to our sleep laboratory undergone polysomnography and morning blood samples were withdrawn for measuring serum leptin concentration. Measurements of C-reactive protein (CRP) was made in 36 patients of them. Mean body mass index (BMI) of the study polulation was 32.4 Kg/m². Mean Apnea-Hypopnea Index (AHI) was 33.5 events/hour. Age, anthropometric measurements and polysomnography parameters were analyzed as determinants of serum leptin and CRP levels. Leptin levels was best correlated with BMI (r = 0.67, p = 0.00), waist circumference (r = 0.66, p = 0.00), neck circumference (r = 0.37, p = 0.0009), desaturation of hemoglobin index (r = 0.40, p = 0.0003), minimum saturation of hemoglobin (r = -0.28, p = 0.011) and the percentage of total sleep time(TST) spent in saturation below 90%(r = 0.29, p = 0.009). There was no correlation with AHI (r = 0.16, p = 0.15) or age(r = -0.12, p = 0.29). In multiple regression analysis, BMI and AHI were responsible for 70% of variation of leptin levels but AHI effect was not independent from BMI in factorial analysis. AHI > 10/hour had a 3.4 fold odds ratio (p = 0.78) of increased leptin levels while AHI > 30/hour had a two-fold odds ratio(p = 0.54). Overweight patients(BMI > 25 Kg/m²) have an 8-fold odds ratio of having increased levels of leptin (p = 0.025). CRP was correlated with BMI (spearman r = 0.62, p = 0.000021), neck (r = 0.42, p = 0.007) and waist circumference (r = 0.50, p = 0.001), minimum hemoglobin saturation (SaO2) (r = -0.46, p = 0.003), desaturation index (r = 0.47, p = 0.002), and percentage of total sleep time spent with SaO2 below 90% (r = -0.42, p = 0.007). It was not correlated with Apnea-hypopnea index(AHI) (r = 0.29, p = 0.69). In backward stepwise multiple linear analysis BMI was the most significant factor(p = 0.0009).In factorial analysis the effect of BMI was not independent from age, or indices of hypoxia. Overweight patients (BMI > 25 Kg/m²) had odds ratio of only 1.86 for high CRP (p = 0.60) but obese patients have more significant possibility of high CRP (OR = 17, p = 0.001). In conclusion, body weight is the major determinant of leptin and CRP levels in patients with OSAS independently from apnea severity. The influence of hypoxia is more significant than that of AHI.

P 052
Approach to a psychoacoustic evaluation of snoring

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Several surgical and nonsurgical procedures for the treatment of snoring have been developed. Their outcome is based on the impression of the bedpartner or the measurement of the sound pressure. Nevertheless the impression of the bedpartner is biased by individual factors which are independent of the snoring sound and the sound pressure doesn’t take in regard the effect of the noise on humans. In our study we tried to evaluate the annoyance of snoring sounds by a psychoacoustic evaluation combining both aspects. 10 patients complaining of loud snoring had
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polysomnography with recording of their snoring. Typical sections of the snoring sound, lasting 30 seconds, were presented to 3 examiners for evaluation (0–100) of their annoyance. The annoyance of all snoring sequences was estimated at 46.9±23.3, the most acceptable snoring sequence at 15±9, the worst at 85±5. The estimations of the examiners concerning a single snoring sequence varied by 8.6±5.0. The psychoacoustic evaluation of snoring seems to be a practicable and promising tool for the measurement of snoring. This new method should make the comparison of different kinds of procedures for the treatment of snoring more effective.

P 053
Prevalence and clinical significance of sleep-related breathing disorder in end stage renal disease
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Aims: Several studies have shown that Sleep-related breathing disorder (SRBD) is quite common in end-stage renal disease (ESRD), and the prevalence has been estimated between 30% and 80%. The effects of SRBD on morbidity and mortality in ESRD patients are not well understood. Here, we present clinical impacts of SRBD in ESRD patients from the viewpoint of subjective daytime sleepiness, complication and prognosis.

Methods: One hundred and sixty seven subjects were studied (male: 96, female: 71, average age 63.8±10.5 year’s old) out of 220 patients who underwent hemodialysis at Dialysis Center of Toyohashi Mates Clinic in Japan from 2001 to 2003. Written informed consent was obtained. SRBD variables were measured from standard polysomnogram (PSG) and subjective daytime sleepiness was evaluated from Epworth sleepiness scale (ESS). Background factors and vascular morbidities were also analyzed. Moreover, mortality follow up study of the subject patients was made during the two years period from the PSG examination.

Results: Average apnea-hypopnea index (AHI/hour) of all the subjects was 25.7±23.0. Ninety-two (55.1%) of ESRD patients had SRBD with AHI of 15 or more. Prevalence of ischemic heart diseases and/or cerebrovascular strokes in the ESRD patient was 44.3% (74 patients), and incidence of these two disorders was significantly increased in proportion to SRBD severity (p*equals*0.0001). Significant confounding factors for 15 or more of AHI in ESRD patients were sex (female, odds ratio-OR: 0.359, 95%CI:0.178–0.726, p*equals*0.0044), age (OR: 1.059, 95%CI:1.021–1.099, p*equals*0.0024) and histories of ischemic heart diseases and/or cerebrovascular strokes (OR: 3.700, 95%CI:1.793–7.637, p*equals*0.0004). Prevalence of ischemic heart diseases and/or cerebrovascular strokes in the subject patients were significantly increased by age (OR: 1.04, 95%CI:1.00–1.08, p*equals*0.042), presence of diabetes mellitus (OR: 3.05, 95%CI:1.45–6.39, p*equals*0.003), presence of SRBD (AHI*gteq*15, OR: 3.02, 95%CI:1.40–6.51, p*equals*0.005), or history of treatment for hyperparathyroidism (OR: 0.23, 95%CI:0.08–0.65, p*equals*0.005). Mortality analysis on elderly (60 years or older) 109 ESRD subjects without CPAP therapy indicated that survival rate of SRBD patients with AHI of 20 or more was significantly lower than that of the patients with AHI less than 20 during the follow up period (p*equals*0.004). Average follow-up period (SD): 806.9 (153.7).

Conclusion: Our results confirmed that SRBD is remarkably high in ESRD patients. Although we could not identify the causative factor for the high prevalence of the disorder, SRBD in ESRD patients was strongly suspected to contribute to the occurrence of ischemic heart disease and/or cerebrovascular strokes. Moreover, SRBD in ESRD patients may act as an aggravating factor for the mortality during their clinical course.

P 054
Attention Networks, Obstructive Sleep Apnea Syndrome and Ageing
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Aim: The main main cause of the impairment of some cognitive functions (memory, attention, etc.) in people who suffer from obstructive sleep apnea syndrome (OSAS) is Excessive Daytime Sleepiness (EDS), due to fragmented sleep and/or to nocturnal hypoxemia. The aim of the present study is to evaluate the effect of OSAS on attention performance, using a rather new task: the Attention Network Test-ANT (Fan et al., J. Cog. Neurosci. 2002, 3: 340–347). ANT is a combination of the cued reaction time (Posner Q.J. Exp. Psyc. 1980, 32: 3–25) and the flanker task (Eriksen & Eriksen Perc. Psychoph. 1974, 16: 143–149). It is designed to measure the efficiency of the three attentional networks 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 hemisphere; 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: 17 untreated OSAS patients (58.2 ±9.3 years), diagnosed by polysomnography and respiratory analysis (AHI = 51.4 ±15.9, BMI = 31.4 ±8.7), 17 healthy adults (57.1 ±8.8 years; BMI = 27 ±6.2) as control group, and 17 healthy students (26.5 ±4.5 years; BMI = 23.7 ±4.2), participated in the experiment. Each subject completed ANT on an IBM compatible computer and was tested in one session lasting about 30 min. A session consisted of a total of 48 practice trials and 3 experimental blocks of 96 trials each. Before performing the ANT their state of vigilance and mood was assessed by means of the Global Vigor-Affect Scale (GVA) and the Stanford Sleepiness Scale (SSS).

Results: The OSAS Group (OG), the Healthy Adults Group (HAG) and the Healthy Students Group (HSG) do not significantly differ as far as Alerting and Orienting networks are concerned. For Executive Control, there is no significant difference between HEG and HSG, while both perform significantly better than OG (p<.01 both comparisons). The mean reaction time shows that OG is significantly slower (p<0.01) than HEG, which in turn is significantly slower (p<0.01) than HSG.

Conclusions: As far as the effects of OSAS on attention are concerned, our data are in favor of a selective impairment of the three attentional 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). Moreover, it appears that ageing does not impair the efficiency of the three attentional networks, but, in general, it slows down the response speed.

P 056
Auditory brainstem response in children with severe obstructive sleep apnea

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Aims: To explore the characteristics of Auditory Brainstem Response (ABR) in severe obstructive sleep apnea patients.

Methods: Auditory Brainstem Response were recorded in 37 severe OSAS patients (study group) and 20 controls.

Results: In the study group, the latency values of waves and were 1.67±0.20 ms 3.87±0.31 ms 5.70±0.31 ms respectively. In the control group, the latency values of waves and were 1.60±0.11 ms 3.81±0.23 ms 5.61±0.23 ms respectively. A statistically significant prolongation were found in the latency values of waves in study group compared to control group (P 0.05). When comparing to the control group, the transmission time between waves and was found to be prolonged and waves to be shortened in the study group. Furthermore, the change was considered statistically significant(P 0.05). A statistically significant elevation was found in response threshold of wave when comparing to control group(P 0.05).

Conclusions: The pathological sleepiness seen in OSAS patients may cause ABR abnormalities, as a consequence of
the chronic hypoxic and hypercapnic status occurring in the brain-stem and cochlear.

**P 057**

**Study of erectile function at syndrome of obstructive apnea of sleep**

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**Aims:** To assess erectile function in patients with syndrome of apnea of sleep.

**Methods:** Polysomnographic study was carried out (GRASS- TELEFACTOR Twin PSG (USA)) with simultaneous monitoring of night erection episodes by application of mercuric NPT-sensor in 14 patients with SOAS and in 14 healthy people, comparable by age.

**Results:** The total time of REM-stages in patients with SOAS decreased. It has been established that in healthy males in the course of a night we marked 4–6 erection episodes, connected with REM-sleep. Total time of spontaneous erections made 1,5 hours (20% of sleep time). In males with SOAS we observed lowered quality and quantity of spontaneous erections during night sleep.

**Conclusion:** We established interrelation between the stage of REM-sleep and night spontaneous episodes of erection. In patients with SOAS we revealed sleep fragmentation, shortening of REM-sleep and correspondingly worsening of erectile function parameters. Using CPAP-therapy made it possible to eliminate apnea episodes, restore sleep structure, which for its turn restores erectile function in patients with SOAS.

**P 058**

**Severe Obstructive Sleep Apnea in Klippel-Feil-Syndrome—a case report**

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**Background:** Obstructive sleep apnea (OSA) is common in patients with congenital malformations of the head and neck.

**Case report:** We report about a 52 year old men with Klippel-Feil-Syndrome (KFS, congenital cervical synostosis, MIM#148900) in whom we diagnosed a severe obstructive sleep apnea syndrome (Respiratory Distress Index > 80/h, minimal oxygen saturation <60%). Clinical examination showed a retrognathia of the upper jaw. A short thick neck and scoliosis of the thoracic vertebral column were due to the vertebral fusion typical for KFS. Restricted opening of the mouth and macroglossia did not allow direct inspection of the pharynx. Via flexible endoscopy we saw a short hard and a thick soft palate and a bony narrowing of the nasopharynx. The base of the tongue was hyperplastic and the larynx was turned to the left in the dorsal part. A mucosal flap originating from the right aryepiglottic fold covered the glottis for more the 90% which caused stridor. Nasal continuous positive airway pressure (nCPAP) up to 20mbar could not really improve OSA. With endoscopy during propofol sleep we could demonstrate total collapse of the pharynx which was reversed with nCPAP. But the positive pharyngeal pressure pushed the described mucosal flap into the glottis and covered it. Limitation of conservative therapy options a tracheostomy (TS) was performed, complicated by the short thick neck and two emergency tracheotomies earlier performed. OSA and its symptoms were completely solved. The patients request for a life without a tracheostoma induced surgical procedures. Partial resection of the base of the tongue was possible with suprahypoidal pharyngotomia, but the laryngeal mucosal flap could not be exposed. Direct endoscopy allowed a minimal look on the larynx and parts of the flap could be resected. The patients stridor was improved, but not the OSA while temporary occlusion of the TS. A repeated CPAP-trial is pending.

**Conclusion:** In KFS multiple narrowings of the upper airway (retrognathia, nasopharyngeal stenosis, macroglossia, malformation of the larynx) can lead to OSA. Diagnostic, conservative and surgical therapy may be complicated in the individual case and need adjusted proceeding. nCPAP-therapy might not be effective when facing multiple stenosis and tracheostomy can not always be avoided.

**P 059**

**Obstructive sleep apnea in women compared to men: clinical differences and underlying factors**

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The disparity of the male to female OSA ratio is likely to depend on various factors (1). Differences in clinical presentation of OSA in women would partially account for OSA being underdiagnosed in women who refer to Sleep Centres (1).

This study is aimed at evaluating clinical patterns of OSA in women and men who had been diagnosed as having OSA at our Sleep Centre during the last two years, on the grounds of symptoms, signs (structured clinical interview plus Epworth Sleepiness Scale) and a full-night monitoring by means of a portable level III polysomnography (Polymesam: MAP Medizin-Technologie GMBH). The evaluation was retrospective and based on an available clinical and instrumental data base.
Preliminary findings concern fifty-five women with OSA (mean age 51.8 years of age, sd 14.1; mean Body Mass Index [BMI] 29 sd 8) compared to 71 men who were similar for age and Body Mass Index.

The clinical pattern of referral in women compared to men was characterized by underreport of typical main OSA symptoms (snoring, witnessed apnoeas, subjective nocturnal gasping and excessive daytime sleepiness) and emphasis of insomnia/minor OSA Symptoms (headache upon awakening, daytime fatigue and depressed mood). Insomnia plus “minor OSA symptoms” were given as the main reason for referral by the 40% of the women with OSA versus the 18% of the men. Insomnia was reported by 11% of the women and 1.5% of the men, awakenings from sleep being largely independent of symptoms of gasping. Grouping women with OSA according to the occurrence of menopause, insomnia was reported more frequently by women with menopause than by the others (15% versus 5%).

Various factors such as different tolerance and awareness of symptoms, biasing effect of comorbidities and different degree of severity and pattern of sleep-related breathing disorders may account for disparity in clinical presentation in women with OSA compared to men.

Polygraphic findings indicate that in our women patients, OSA is less severe than in men of similar age and BMI (AHI: 15.7, range 6-74 versus 26.3, range 6-94; p < 0.005 at t student test) and that the temporal occurrence of apnoeas/hypopneas throughout the night is “REM-like” more frequently than it is in men (32.7% versus 7.0%; p < 0.001 at chi square test).

All in all our preliminary findings indicate that different pattern of sleep-related breathing abnormalities along with the interfering effect of menopause per se on sleep continuity may partially account for differences in clinical pattern of OSA in women compared to men.


P 060
Romanian experience in using CPAP for Sleep Apnea Syndrome

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Aim: The aim of the study was to evaluate the role of CPAP in the treatment of sleep apnoea syndrome (SAS).

Methods: We included 101 SAS patients diagnosed by poligraphy in a Romanian special designated Centre, in a period of 1 year. A score of symptoms, apnea-hipopnea index (AHI), and the presence of UPPP were determined pre and post CPAP.

Results: 90.09% of patients were male, median age was 52.36 years. 18.81% of patients underwent UPPP before therapy with CPAP, from whom 84.21% were considered therapeutic failure. 78.94% of UPPP patients had AHI > 30, being classified as severe SAS. 51.48% of patients without UPPP had AHI > 30 and a median score of symptoms (SS) of 41 before CPAP. Only 4.87% of patients with CPAP without UPPP (82) had therapeutic failure while 56.09% being under current evaluation. The median SS after CPAP for severe SAS patients was 24.54%, an important decrease.

Conclusions: Because the therapy with CPAP it is not financial supported by the National House of Health Insurance, the selection of patients who could benefit from CPAP therapy was made by the level of severity of SAS only for patients who could afford the expenses alone. Also, we could note that in the past years the indications for UPPP were not reliable made in Romania, thus predisposing at therapeutic failures. A less compliance and many technical problems with CPAP after UPPP were noted.

P 061
The experience of obstructive sleep apnoea syndrome in Romania

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Aim: The aim of this study was to evaluate the patients diagnosed with obstructive sleep apnoea syndrome (OSAS) by poligraphy in Romania.

Methods: In this retrospective study were included 698 patients with clinical suspicion of SAS referred to our Centre of poligraphy in a period of 8 years. They underwent a poligraphic test and a symptom score was made. The apnea/hipopnea index (AHI), associated diseases, the smokers were determined and the relative frequencies were calculated.

Results: 81.23% were males, median age was 50.3 years. 61.89% were smokers. 3 categories were identified by apnea-hipopnea index (AHI): 23.78% (166 patients) had AHI <5 and inirmed the diagnose of SAS. 11.74% had AHI =5-9; 15.47% had AHI =10-20; 12.03% had AHI = 20-30 and 36.96% had AHI >30. 86.53% of all patients were obese. 18.22% of OSAS patients (450 patients) had overlap syndrome, while 12.44% of OSAS patients had diabettes mellitus. Only a small proportion of patients had endocrine diseases: 2.88% and cardiac failure or aritmia: 15.77% and 4% respectively. The cardiac ischemic disease and blood hypertension incidence was 41.33% and 42.88% respectively. Almost a half of the OSAS patients had septal nose deviation, 18.88% with surgical interventions. 64.88% of OSAS patients had palate wall prolapsed and uvulo hypertrophy, 6.84% being operated. 29.33% and 36.88% of patients had adipose infiltration of pharynx and chronic rhinitis.

Conclusions: It would be of benefit that the patients from gray zone be tested by polysomnografi for better diagnosis.
It is important to note the high proportion of smokers among OSAS patients and the high incidence of obesity, thus conducting to cardiac ischemic disease and blood hypertension.

**P 062**

**Evaluation of Pharyngeal Volume and Compliance of OSAHS Patients Using 3D CT and Volume Measurement**

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A new imaging method was designed to evaluate both baseline caliber and compliance in normal individuals and OSAHS Patients, and to localize the obstructive sites in OSAHS patients. 7 normal individuals and 13 OSAHS patients were studied. Critical closing pressure (Pcrit) and minimally effective therapeutical pressure (Peff) were measured and computed tomography scan of pharynx was performed during wakefulness and drug-induced sleep with Pcrit, 0 cmH2O and Peff being given through a nose mask system. 3D images of pharyngeal airway were reconstructed, and volume of each subdivision of pharynx was measured. Volume, average area and compliance of each subdivision were compared between the two groups. Anatomy of pharynx could be easily understood on the virtual endoscopic view. On an air-mode view of 3D image, the outline of pharynx was shown as transparent tubal structure, on which the narrowing collapse of airway at any level or any direction can be easily identified. During wakefulness the average area of the upper and middle part of pharynx was significantly smaller in OSAHS patients than in normal individuals respectively. During sleep this difference was more obvious at the upper part and middle part. The compliance of the middle part of pharynx was significantly higher in OSAHS patients than in normal individuals. The date suggested that OSAHS patients have a narrower and more collapsible pharynx compared to the normal subjects. The method of our study is valid to evaluate both morphology and function of upper airway.

**P 064**

**Influence of CPAP therapy on leftventricular Hypertrophia in patients with OSAS and Hypertension**

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Introduction: Patients with severe sleep apnea suffer frequently from hypertension. Only few data are available about the echocardiographic changes in these patients during longterm therapy with CPAP.

Methods: We examined 70 patients with severe OSAS (age 54.4±12.5, BMI 41±16 kg/m2, AHI 53±35/h). There were treated with CPAP on average for 5.3 years. Daily usage of CPAP was 5.3 h/day. As a sign of cardiac
changes we measured the thickness of the leftventricular posterior wall and the interventricular septum by m-mode echocardiography.

Results: With CPAP the number of respiratory events was reduced to normal range (AHI 3/h). In addition the echocardiographic parameters changed to normal range as well.

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<th>Start</th>
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Discussion: Continuous use of CPAP normalised blood pressure and induced a decline of leftventricular hypertrophia.

P 065
Obstructive sleep apnoea (OSA) in males and females: impact of age

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It is generally accepted that prevalence of OSA increases with age. The aim of this study was to evaluate impact of age on incidence and severity of OSA. In 3785 subjects evaluated at our Sleep Laboratory, OSA was confirmed in 1657 (1426 males and 231 females) [43.8%], mean age 52.7±10.5 years. OSA subjects presented with obesity (mean BMI- 32.9±6.4 kg/m²) and severe disease (mean AHI-42.4±24.5, mean SaO₂-89±7%, T90-33.8±31.6%). To assess relations between OSA and age, patients were divided into three groups: group 1 ≤44 yrs (343 subjects; 20.7%), group 2, 45-64 yrs (1071 subjects; 64.6%) and group 3 ≥65 years (243 subjects; 14.7%). Comparison of those groups was done, separately for males and females.

Males: in group 1 consisted of 325 subjects (22.8%), group 2 of 920 (64.5%) and group 3 of 181 (12.7%) subjects. Youngest males were more obese and presented very severe OSA. BMI was 37.7±10.1# (group1), 34.1±7.5 (group 2), 31±6 # kg/m² (group 3), (#−p=0.02). AHI in group 1-50.6±36.2, in group 2- 38.5±24.4, and 33.5±17.6, in group 3 (NS).

Mean SaO₂ (%) was similar in all groups (88±8.6, 88.4±6.6, 87.6±8.6%, respectively in group1,2,3; NS). Subjects from group 1 and 2 spent more time in desaturation below 90% (T90) than group 3 (34±40.9, 32.6±33.1, and 25.3±29% respectively in groups 1,2,3; NS).

Conclusions: OSA was most frequent in males and females in age span 45-64 years. Most severe disease was found in youngest males and females, mildest OSA was diagnosed in the oldest subjects. Diagnosis of OSA in subjects ≥65 years was two times higher in females (26.8%) than in males (12.7%).

P 066
Reliability of self-assessed snoring: questionnaire vs polysomnography (PSG)

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In a study assessing prevalence of sleep disordered breathing (SDB) in a representative population sample of Warsaw (676 subjects; 320 F and 356 M), mean age 56.6±8.2 years, all subject filled sleep questionnaire before PSG. Aim of the study was to compare questionnaire data with snoring registered during PSG. The results of questionnaire (Q) were as follows: non-snorers-171 (25.3%), moderate snorers-221 (32.7%) and habitual snorers -284 (42%). According to PSG results, studied sample was divided into 6 groups: gr. 0-non snorers (Q) and non snoring on PSG (82 subjects), gr.1-moderate snorers (Q) and snoring on PSG (136 subjects), gr.2- habitual snorers (Q) and snoring on PSG (236 subjects), gr.3-moderate snorers (Q) and non snoring on PSG (85 subjects), gr. 4-habitual snorers (Q) and non snoring on PSG (48 subjects), gr. 5- non snorers (Q) and snoring on PSG (89 subjects). The best agreement between questionnaire and PSG was found in habitual snorers-83.1% of them snored on PSG. 61.5% of moderate snorers snored on PSG and only 48% of non-snorers did not snore on PSG.

Subject from group 2 had highest AHI (9.6±12.5) and BMI (30.1±5.2 kg/m²). They spent more time in desaturation below 90% (T90)-11.7±20.6%. Epworth sleepiness score was also highest in group 2 (7.6±4.2 points) and mean SaO₂ was lowest in this group (92.9±2.5). Conclusions: More than 80% of subjects reporting habitual snoring snored during PSG. Those subjects presented with obesity, higher Epworth score, more...
apnoeas and lowest mean SaO₂. Our study confirmed that self reported snoring is very reliable symptom of OSA.

P 067
Maxillo-mandibular distance recording as a marker of non apneic sleep-disordered breathing
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Background: In clinical practice, measurement of breathing efforts during sleep is needed to quantitate sleep-disordered events inaccessible to direct evaluation of nasal or thoraco-abdominal activity. This is the case in heavy snoring, Respiratory Effort-Related Arousals (RERA) and Upper Airway Resistance Syndrome (UARS). More sophisticated analyses of nasal pressure curves, thoraco-abdominal movements and central nervous system (CNS) arousals are proposed to detect these events without the cumbersome gold standard oesophageal pressure recording (Pes).

Aims: We observed that a continuous recording of the distance between 2 points situated on the vertical midline on both sides of the lips, a measurement of the opening of the mouth, reflected breathing efforts during sleep when 2 conditions were met: (1) evidence of mandible oscillations in the range of the respiratory frequency (0.15–0.3 Hz); (2) a lowering of the mandible greater than 20% of maximal voluntary opening of the mouth. This method allowed us to detect efforts associated with apneas and hypopneas. The present study was outlined to define the pattern of mandible movements associated with UARS.

Method: Fifteen UARS patients, 9 women and 6 men (mean age: 42-year-old ±16.5 SD), entered the study. The UARS diagnosis was based on the history (chronic fatigue, excessive daytime sleepiness) and polysomnography (PSG). An Upper Airway Resistance Event (UARE) was settled when on PSG, (a) a progressive Pes inspiratory decrement below -15 cmH₂O occurred; (b) ended by an abrupt increase of Pes associated with a CNS arousal; (c) without any feature of apnea or hypopnea. UARS was confirmed when (a) the AHI was lower than 10/h; (b) the Arousal-RDI index was higher than 20/h. A Maxillo-Mandibular distance Recording (MMR) was obtained by using 2 coupled small magnetometers fixed, one on the chin, and the other on the forehead, on the midline of the face. The tracing was integrated in a complete PSG along with the Pes.

Results: On the MMR, UARE was indexed by progressive lowering of the mandible driven by continuous inspiratory (oscillatory) superimposed movements. The lowering ended by an abrupt elevation coincident with an arousal. Apneas and hypopneas differed from UARE (1) by a non linear evolution of the lowering; (2) by a shorter duration (18±10.5 vs 216±166 s, p<0.01), and (3) by a less abrupt elevation of the mandible ending the progressive lowering (7.4±3.1 vs 1.2±0.5 breaths, p<0.01). During UARE, the mandible depression associated with oscillations in the respiratory frequency band was initiated at a Pes level of −11.7±7.4 cmH₂O and ended at −30±12.3 cmH₂O.

Conclusions: (1) A recording of the opening of the mouth during sleep by a distance-meter with sensors fixed on 2 points on the midline of the face provides a surrogate of Pes for the diagnosis of UARS; (2) the abrupt elevation (<2 breaths), following the lowering of the mandible, is coincident with UARE arousal.

P 068
Effects of Obstructive Sleep Apnea and Subsequent Treatment on Mood and Cognition
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Aims: Nasal Continuous Positive Airway Pressure (CPAP) is the standard treatment for Obstructive Sleep Apnea with well documented efficacy. Some patients are unable to tolerate CPAP for various reasons. One of the alternative treatments is Maxillo-Mandibular Advancement (MMA) surgery. The purpose of this study is to compare the effectiveness of CPAP to MMA with respect to mood changes and cognitive dysfunction.

Methods: Eight OSA patients who qualified for surgical treatment with MMA were treated with CPAP during the waiting period for the surgery. All patients underwent evaluation of sleep (overnight Polysomnography and daytime Multiple Sleep Latency Test), mood (Hamilton Depression Scale, HDRS; Beck Depression Inventory, BDI; Symptom CheckList-90R, SCL-90), cognitive complaints (Cognitive Failures Questionnaire, CFQ) and subjective symptoms (Epworth Sleepiness Scale, ESS and Functional Outcomes of Sleep Questionnaire, FOSQ). The tests were carried out at enrolment, after 3 months of CPAP treatment, and 6 months post MMA surgery.

Results: Results were analyzed with paired t-tests. Mean Apnea-Hypopnea Index (AHI) decreased significantly with CPAP and, despite a slight significant increase, remained low after MMA (M=59.8, 0.26, and 6.0 respectively, P’s<.001 vs baseline). Mean MSLT increased at the 3 time points, but the change was not significant (M=7.7, 12.5, 9.4). Subjective ratings of sleepiness (ESS) did not significantly improve until after surgery (M=15.4, 10.6, 5.1, p<.001). Self-report measures of depressive symptomatology showed improvement (BDI=9.4, 6.5 and 0.5, P’s<0.001); SCL-90 DEP
subscale mean T=59.9, 55.4 and 48) with significant symptom decrease following the surgery compared to CPAP. Measures of subjective global impairment also showed improvement (FOSQ=14.8, 17.5 and 19.5; SCL-90 GSI subscale T=59.6, 54.4 and 48.4). The frequency of self-reported cognitive failures, a measure of cognitive efficiency, decreased (CFQ=40.4, 33.8 and 30.5) although the changes were not statistically significant.

Discussion: The results confirm previous reports of the effectiveness of CPAP in the treatment of OSA and associated mood symptoms. In addition, outcomes following MMA appear as positive or better, particularly in self-reported mood and sleepiness symptoms. Despite the positive changes in self-reported sleepiness, mood and global functioning, the cognitive changes were not as dramatic. This may be attributed to differences in instrument sensitivity or longer time required for cognitive function recovery. Alternatively, OSA may result in lasting cognitive impairment despite adequate treatment. The ongoing study will include additional subjects to confirm the robustness of these findings, as well as compare these findings to long-term outcome from surgical intervention.

Conclusions: A short 6 point questionnaire helped identify diabetic patients at risk for SDB. Home Screening was highly positive for SDB and Auto-titration was well tolerated and reduced the RDI significantly.

Clinical Plans: Each experimental patient is scheduled for in lab Polysomnography and confirmatory CPAP titration will occur at that time.

P 070
Prevalence of Cheyne-Stokes Respiration (CSR) in patients with ischemic and non-ischemic congestive heart failure (CHF)
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Prevalence of CSR in patients with CHF is very high, ranging from 30-50%. Obstructive sleep apnea (OSA) seems to occur less frequently in these patients. It is unknown if there are differences in the prevalence of sleep disordered breathing (SDB) between patients with ischemic and non-ischemic CHF. To determine the prevalence of SDB in patients with stable CHF we performed an ambulatory polygraphy (Embletta, ResMed) in 102 consecutive patients with an ejection fraction (EF) < 45%. Three of these patients were excluded due to an insufficient recording quality. Patients were assigned to CSR (AHI > 10/hour; > 50% of central events), to OSA (AHI > 10/hour; > 50% of obstructive events) or to no relevant SDB (AHI < 10/hour). 99 patients (age: 54.7 ± 13.6; BMI: 27.6 ± 5.4; EF: 28.0 ± 9.6; AHI 21.7 ± 15.0) completed the study, non-ischemic CHF was present in 56 patients (age: 53.2 ± 13.7; BMI: 28.4 ± 6.3; EF: 26.6 ± 8.8; AHI: 15.5 ± 14.4) and ischemic CHF in 43 patients (age: 66.7 ± 9.1; BMI: 26.3 ± 3.5; EF: 30.8 ± 9.8; AHI: 20.3 ± 15.3). In the whole group prevalence of CSR was 33% and prevalence of OSA was 33% as well. CSR was less prevalent in patients with non-ischemic compared to patients with ischemic CHF (23% vs. 38%). In conclusion prevalence of SDB in patients with stable CHF is very high, but OSA is found more frequently than previously reported. Many patients show both pattern of SDB. Coronary artery disease seems to be a risk factor for developing CSR in this group of patients.

P 069
Screening for Sleep Disorderd Breathing in a VA Diabetes Clinic. Use of a questionnaire, a Home diagnostic device, and an automatic Pressure Titration Device
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Department of Pulmonary and Sleep Medicine

The association of Sleep Disordered Breathing (SDB) and Diabetes has become more widely recognized over the past few years. Other Comorbid Conditions commonly occur with SDB including Hypertension and other Cardiovascular Diseases. Obesity is a condition common to all these conditions. Control of the Diabetes is more difficult in the presence of Diabetes. We wanted to evaluate a care path which included home screening for SDB and home Automatic CPAP titration.

Methods: We screened consenting Diabetic Patients using a 6 point questionnaire. Three or more points had previously been shown to yield a high incidence of SDB in a VA population. We assigned these positive patients to a home screening program using a Watch Pat™. Those qualifying for treatment under the current US Medicare Guidelines were titrated with an AutoSet™ Device.

Results: The 6 point questionnaire yielded a significantly elevated response rate in this Diabetic Population. Home Screening for SDB yielded a high RDI in this population. The Automatic CPAP titrator was successful in reducing the RDI and there was good patient tolerance.

One educational session can improve objective sleep quality and mask tolerance of patients during Positive Airway Pressure titration
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Aims: To evaluate if an educational session by PSG technician during the night of PAP titration can improve objective sleep quality and mask tolerance of patients in the sleep laboratory.

Methods: The educational program for PSG technician started in September/2003 and its protocol included: (1) patient education about OSAHS, its consequences and treatment; (2) CPAP/BiPAP titration, therapy, and side effects; and (3) patient training with PAP equipment and selection of mask type before the beginning of PSG hook up preparation. Patients were divided in two groups: those previously referred to PSG for CPAP/BiPAP titration (March to August/2003: n=699) and those referred to PSG for PAP titration after the beginning of protocol (March to August/2004: n=782).

Results: Demographic data of both groups of patients were similar (2003 vs. 2004): male and female proportion (76:24 vs. 75:25), age (mean ± SD) (53 ± 12 vs. 52 ± 12 years) and BMI (31 ± 6 vs. 31 ± 6 kg/m²). After the educational session, the number of patients that did not tolerate nasal mask during PSG recording was lower (80 vs. 44) (p=0.001). PSG data were different (p<0.05) according to: TST (312 ± 81 vs. 326 ± 85 min), sleep efficiency (74 ± 17 vs. 77 ± 14%), Sleep latency (22 ± 24 vs. 18 ± 29 min), S1 (8 ± 8 vs. 6 ± 5%), S3 + 4 (19 ± 11 vs. 21 ± 13%), REM sleep (17 ± 9 vs. 18 ± 9%), wake after sleep (106 ± 68 vs. 93 ± 58 min).

Conclusion: One session of patient education by PSG technician can improve objective sleep quality and nasal mask tolerance during the night of PAP titration. It could be an efficient intervention to improve PAP compliance.

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P 072
Validation of microMESAM as screeningsystem for Sleep Apnea Syndrome

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Background: MicroMESAM is a newly developed screening device based on respiratory pressure measurements via nasal canule, allowing automated analysis of apnoeas, hypopnoeas and snoring. Wang et al1 concluded that it is a suitable screening device for Sleep Apnoea Syndrome (SAS). To validate the device we compared microMESAM data with Polysomnographic (PSG) data of patients possibly suffering from Sleep Apnoea Syndrome.

Methods: In 40 consecutive patients referred to our sleep-lab, microMESAM and PSG were performed simultaneously during the same night. SAS, diagnosed with microMESAM was defined as Apneu/Hypopneu (A/H) index > 15/h. SAS diagnosed with PSG was defined as A/H index > 15/h or desaturation index > 10/h.

Results: In 7 patients microMESAM data could not be analysed, because of technical problems due to the combination of the nasal canule of the microMESAM with the nasal thermistor of the PSG. The results of the remaining 33 patients are summarized in the table. The sensitivity of the microMESAM was 100% (95% c.i. 76–100%) and its specificity 47% (95% c.i 24–71%) Micro-MESAM Apnoea/Hypopnoea index correlated strongly with PSG Apnoea/Hypopnoea index (R=0.956, p=<0.001). MicroMESAM snore events correlated moderately with PSG arousal index (R=0.593, p=<0.001).

Conclusions: MicroMESAM is moderately specific but highly sensitive in detecting Sleep Apnoea Syndrome. It is suitable as screening device for Sleep Apnoea Syndrome. The results support earlier findings1.

Table: Count Micromesam (MM) Sleep ApneuSyndrome (sas)* Polysomnographic (PSG) Sleep Apneu Syndrome cross tabulation. Fisher’s exact test (2-sided): p=0.003

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Reference

P 073
The role of insomnia in CPAP acceptance and compliance

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Sleep apnea patients may not utilize CPAP for a variety of reasons: 1. They may refuse to be seen for a sleep consultation, 2. Once seen, they may refuse to be studied with CPAP, 3. During polysomnography, they may refuse or prematurely terminate the CPAP titration, 4. They may refuse to accept or fill a CPAP prescription, 5. Financial concerns may preclude them from obtaining or continuing
CPAP. 6. They may refuse to wear it for psychological reasons (claustrophobia, body image, etc) or for medical reasons (nasal symptoms, mask leak, pressure intolerance, etc), 7. They may have another underlying sleep disorder (restless legs/PLMs, insomnia) that might inhibit CPAP use. Anecdotal experience suggests that patients with insomnia and OSA have reduced CPAP acceptance and compliance. We explored the effect of a diagnosed insomnia disorder in a group of OSA patients considered to be CPAP candidates.

We performed a retrospective chart review of 207 consecutive patients who underwent a split night PSG with successful CPAP titration. Twenty-four of 207 (12%) had an initial sleep consultation diagnosis of insomnia (various types). Compared to the 183 patients without insomnia, those with insomnia tended to be older (58 yr. vs 54), were more often female (46% vs 27), and had a lower AHI (26/hr vs 43). Insomnia did not prevent adequate sleep evaluation, (Total sleep time with CPAP 156 min vs 179). All 24 patients were given a CPAP prescription and 19 (79%) filled the prescription. Follow-up compliance was assessed by questionnaire. Fifteen of the 19 patients responded (2 deceased, 2 unreachable) with average length of follow-up 46 months. Fourteen of 15 patients (93%) continued to use CPAP for an average of 5.5 hrs/night (4.5 8 hrs).

A diagnosed insomnia disorder does not commonly accompany OSA. Insomnia patients tend to be older and have less severe OSA. Insomnia did not prevent adequate sleep evaluation. Acceptance and compliance with CPAP appears to be satisfactory in patients with insomnia and OSA.

**P 074**

Quality of life in patients with Sleep Apnea Hypopnea Syndrome Effect of three-month CPAP application

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Patients with Sleep Apnea Hypopnea Syndrome (SAHS) have a poor Quality of Life (QoL). The aim of the study was to assess QoL in SAHS patients and to examine the influence of CPAP therapy over time.

Patients-Methods: In 106 individuals (91 men, 15 women, mean age 50±10.3 years), with reported breathing disorders in sleep, a polysomnography was conducted. QoL was assessed by the Short Form-36 (SF-36) questionnaire, and reported sleepiness by the Greek version of Epworth Sleepiness Scale (ESSgr). According to the polysomnography results and clinical features, the appropriate therapy was prescribed. QoL was reassessed after three months on CPAP therapy.

Results: In 87 patients AHI was 57±22.4/h and ESS 12.9±5.6. All of them were prescribed a CPAP therapy, but 11 of them refuse to receive it. Nineteen patients had an AHI<5/h (AHI 2.9± 2/h) and served as controls. SF-36 scores were lower in SAHS patients, in comparison to controls, in all domains (physical function, physical role, pain general health (p<0.05), emotional wellbeing, emotional role, social function, and energy/fatigue) At the first trimester, changes in QoL of SAHS patients were observed. Those patients under CPAP showed significant (p<0.05) improvement in all SF-36 domains except pain, and in some domains they even exceeded controls’SF-36 scores. Reported sleepiness improved (ESS 0.8±2.5, p<0.001) Patients who refused to start a CPAP therapy had lower SF-36 scores over time in most SF-36 domains.

Conclusion: SAHS patients have a poor QoL, in comparison to individuals with normal respiratory function during sleep. CPAP use improves QoL even from the first trimester. Patients, who do not apply a CPAP device, tend to report worsened QoL over time.

**P 075**

Blood pressure level, metabolic parameters and apnea/hypopnea index in patients with different ACE genotype

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Objective: The obstructive sleep apnea syndrome (OSA) is the well-recognized risk factor of cardiovascular diseases, what resulted in introduction the term of syndrome Z by I.Wlkox in 1996, which combines it with metabolic syndrome. The present study investigated association of blood pressure (BP) level with apnea/hypopnea index and metabolic parameters in patients with different types of ACE genotype.

Patients and Methods: We examined 73 patients (42 male and 31 female) with mild to moderate hypertension. The mean age was 52.1±9.1, the mean office BP 155±20.7 mm Hg and 95.8±12.1 mm Hg. All patients proceeded blood analysis of biochemical metabolic syndrome markers, 24-h BP monitoring (SpaceLabs 90027), and diagnostic polysomnography (Embletta pds., 2001 Australia) with determination apnea/hypopnea index. Determination the I/D polymorphism of ACE gene was performed by a standard technique.

Results: The genotype distribution of ACE gene was the following: genotype II was observed in 22 patients (11 male
P 076
ENDO CUT® Surgical Handpiece Designed for radio Frequency Adenoidectomy for Sleep Breathing Disorder in Pediatric Patients

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We presented our experience of performing adenoidectomy with ICC200, a radio frequency surgical system which could provide both ENDO CUT and soft coagulation modes. ENDO CUT handpiece was designed simulating the Beckmann’s adenoidectomy. We used ENDO CUT mode and soft coagulation mode in ICC 200 made by ERBE Cooperation, Germany. ENDO CUT mode is possible to reduce bleeding by repeating coagulation and cut automatically. And then soft coagulation mode can prevent carbonization at a peak voltage less than 190V. Our results from all 8 cases showed that less bleeding, shortening of operation time could be achieved by using this device. The surgical skill was found to be similar to traditional adenoidectomy, and the residual adenoid tissues approaching to the posterior edge of nasal septum still required to be removed with a forcep or punch. Soft coagulation is especially helpful to control the bleeding in this area, and also effective for the bleeding from surgical wound produced by ENDO CUT.

P 077
The course of Sleep Apnea Hypopnea Syndrome (SAHS) without therapy over time

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Aim of this study was to evaluate changes in general health and respiratory function in sleep and awake in SAHS patients who did not receive therapy.

Patients/Methods: Forty-four patients (aged 51.84 ± 10.8 yrs) underwent respiratory function evaluation and polysomnography and answered questionnaires about their sleep habits and comorbidities (To). They were examined again after 6 to 152 months (Tx:37.58 ± 30.7 months). An increase in AHI greater than 30% (AHI = (AHITx-AHITo)/AHITo > 30%) was the cut-off point to assess significant deterioration of breathing function during sleep.

Results: The prevalence of SAHS-associated reported symptoms declined (especially snoring, p < 0.05). An increase in the prevalence of cardiovascular diseases (especially arterial hypertension) and Diabetes Mellitus was also observed (p < 0.05). No significant changes in BMI, Epworth Sleeping Scale, AHI, minSaO2 and respiratory function in awake, assessed by spirometry and arterial blood gases analysis, were observed. In twenty patients (45.45%), who showed an increase in AHI > 30%, AHI significantly correlated with AHITo (p < 0.05). In these patients, AHITo was 27.17 ± 13.02/h, whereas, in those with AHI < 30%, AHI was 46.84 ± 20.3/h (p < 0.05)

Conclusion: SAHS patients tend to report less severe symptoms over time, despite the observed deterioration of breathing function in sleep. This regression is more profound in patients with mild SAHS. In accordance to literature, our data suggest that cardiovascular diseases, especially arterial hypertension and diabetes mellitus, increase over time.

P 078
Impact of CPAP Treatment on the Muscular Tone of the Tongue

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Upper airway dilator muscles play an important role in the pathogenesis of the obstructive sleep apnoea syndrome. The main working hypothesis is that CPAP treatment will restore the tonicity of the dilator muscle of the upper airway (m genioglossus being the major cause of apnoea), which can be objectivized by myotonometrical measurements (MM). The present study compares tissue property changes of the lingual muscle between the non-treated apnoeics (10 subjects-aged 30–45 y) and ...
the same patients’ after a 12-month CPAP treatment. The subjects underwent polysomnography before and after CPAP treatment at the Sleep Laboratory of the Tartu Ear Clinic. The MM were performed while the subjects were awake. The tongue tissue response after a brief mechanical impact on the sublingual surface was expressed as damped oscillation. The frequency of the damped oscillations characterizes tissue stiffness, and the logarithmic decrement of the damped oscillations characterizes tissue elasticity. The result of MM indicated that patients with a 12-month CPAP treatment show an increased elasticity of the tongue, which is numerically expressed as a decreased decrement (before 3.0 ± 0.2 and after 2.1 ± 0.3) and decreased stiffness (before 14.1 ± 0.7 Hz and after 11.5 ± 0.2 Hz). Consequently, the biomechanical properties of the tongue restore during the CPAP treatment at the Sleep Laboratory of the Tartu Ear Clinic. The MM were performed while the subjects were awake. The tongue tissue response after a brief mechanical impact on the sublingual surface was expressed as damped oscillation. The frequency of the damped oscillations characterizes tissue stiffness, and the logarithmic decrement of the damped oscillations characterizes tissue elasticity. The result of MM indicated that patients with a 12-month CPAP treatment show an increased elasticity of the tongue, which is numerically expressed as a decreased decrement (before 3.0 ± 0.2 and after 2.1 ± 0.3) and decreased stiffness (before 14.1 ± 0.7 Hz and after 11.5 ± 0.2 Hz). Consequently, the biomechanical properties of the tongue restore during the CPAP treatment in young patients. The study was supported by the Estonian Science Foundation (GARPS5842).

P 079
Sleep-Disordered Breathing Surgery: Phase I Results in our Personal Experience

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Aims: Evaluation of personal results in Phase I Surgery.

Methods: Retrospective evaluation of two groups: GROUP A (n=102) Palate surgery; GROUP B (n=89) Hyoid Suspension and/or Genioglossus Advancement. Outcomes after 6 months were divided into: 1.CURED: post op RDI <10 + ESS <10; 2.CARDIOVASCULAR PREVENTED: post op RDI<20 + ESS<10; 3.IMPROVED: post op RDI/ESS < pre op RDI/ESS; 4.UNCHANGED: post op RDI & ESS = post op RDI & ESS; 5. WORSENED: post op RDI/ESS > pre op RDI/ESS. SUCCES DEFINITION = 1 + 2.

Results: UPPP + Tonsillectomy scored 78% of success; success rate was 86% for Hyoid and 75% for Genioglossus; only 50% for H+G.

Conclusions:
1. palate surgery if properly selected may fix a significant number of OSAH cases;
2. UPPP + Tonsillectomy is the most efficient procedure in oropharyngeal area;
3. Hyoid suspension in our hands was the best procedure in hypopharyngeal area;
4. RDI & BMI cutoff <30 is crucial for Phase I selection ad final success.

P 080
Sleep-Disordered Breathing Surgery: Phase II Results

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1ENT Unit, University of Pavia in Forlì, Morgagni & Pierantoni Hospital, Forlì (Italy); 2Sleep Lab, Neurological Clinic, University of Bologna Italy

Aims: Evaluation of our experience in Phase II surgery according to Stanford protocol, modified.

Methods: Retrospective evaluation of maxillo-mandibular advancement (MMA), Tongue-Base Reduction with Hyoid-Epiglottoplasty (TBRHE) and Skin Lined Tracheotomy (SLT). Evaluation: PSG and ESS before and after 6 months. Outcomes were divided into: cured: post-op RDI <10 + ESS<10; cardiovascular prevented: post-op RDI<20 + ESS<10; improved: post-op RDI/ESS < pre-op RDI/ESS; unchanged: post-op RDI/ESS = post-op RDI/ESS; worsened: post-op RDI/ESS > pre-op RDI/ESS.

Results: The outcome of 4 TBRHE, with pre-op average RDI 66.5 and ESS 15, is 3 improved and 1 unchanged. In opposite the results in 15 MMA pts, with pre-op average RDI 55.8 and ESS 11, was excellent (15/15 cured). SLT was adopted in only 4 pts with CPAP intolerance, severe RDI and BMI, severe anaesthesiological risk or cerebropathy), obtaining complete recovery and satisfying compliance.

Conclusions: Our TBRHE results was not excellent. MMA is the best procedure available in Phase II and it is the gold standard in case of severe OSAS in morbid obesity. After the tracheotomy, MMA is the single procedure with the maximum expectance of cure.

P 081
Maxillo Mandibular Advancement for Severe Oshas in Obese Patients: Personal Experience

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Aims: Retrospective evaluation of Bimaxillary Advance ment in OSAHS Surgery.

Methods: Evaluation of 17 maxillo-mandibular advancements for severe OSAHS in significant obesity. 15 out of the 17 received Bimax as first and unique surgical procedure. Basic selection criteria were RDI >30 and BMI >30. Two cases were treated as salvage surgery after a complete Phase I failure. All the cases received the same diagnostic protocol including: 1. Sleep Medicine complete work up 2. ENT complete work up 3. Imaging 4. Neuropsychological Test Battery. 5. Oral Surgeon evaluation. Fiberoptic intubation
was necessary in 14 patients. Tracheostomy was performed in all the cases.

Results: All the pts were discharged within 1 week and without tracheostomy. 100% were cured (RDI<10 and ESS<10) with a mean post op RDI of 4.7 and mean post opp ESS of 7.0. Perceived Bimax pain was significantly lower than UPPP pain. Long lasting paresthesia in lip, chin and cheek along with a minimal degree of malocclusion were the most common post op complaints. 16 out of the 17 patients would go through the operation all over again.

Conclusion: Bimax is a very effective operation for severe & obese cases, with a good patient compliance.

P 082
High Prevalence of Sleep Apnoea (SA) Syndrome in Patients with Paroxysmal Atrial Fibrillation (pAF)-A Study Using Questionnaires and Transthoracic Impedance Measurement (TTI) Integrated in a Holter ECG System

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Background: A strong association of atrial fibrillation (AF) and obstructive sleep apnoea (SA) has been documented recently by Gami et al (Circ 2004) by means of Berlin questionnaire. Additionally our group used a new automatic detection algorithm based on transthoracic impedance measurement (TTI) integrated in a standard Holter ECG (CardioMem 3000, getemed, Teltow, Germany) to detect SA. The method was validated with polysomnography with a 0.80 sensitivity, specificity 0.93, positive predictive value 0.78 and negative predictive value 0.93 before.

Purpose of the study: Prospective evaluation of the association of SA in unselected pts. with a history of pAF admitted to a university cardiology department for any reasons.

Methods: PAF patients were not known to suffer from SA so far. An impedance apnoe hypopnoe index ≥10 as detected with TTI was defined positive for SA. The Berlin questionnaire (validated for the detection of obstructive SA) and Epworth sleepiness scale (with a cut-off value of ≥9 for SA positive) were used.

Results: 30 consecutive pts. (13 f), mean age 63±11 y,14 with structural heart disease (8 valve disorders, 5 CAD, 1 ASD), mean EF 57±7% with a history of 3.1±5.6 y (range 0.1–25) of paroxysmal atrial fibrillation (17±26 episodes/mon, range 1–90) were studied. A high prevalence of SA was shown in the study population highlighting the clinical relevance of screening AF patients for SA.

<table>
<thead>
<tr>
<th></th>
<th>Transthoracic Impedance Holter recording</th>
<th>Berlin Questionnaire</th>
<th>Epworth Sleepiness Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA positive</td>
<td>13/30</td>
<td>13/30</td>
<td>14/30</td>
</tr>
<tr>
<td></td>
<td>43%</td>
<td>43%</td>
<td>47%</td>
</tr>
</tbody>
</table>

Conclusion:
(1) Our results prove a high prevalence of SA in patients with pAF.
(2) These results were confirmed by the questionnaires as with the TTI system integrated in a Holter ECG.
(3) Further studies are needed to elucidate the pathophysiological link between pAF and SA.
(4) TTI integrated in a standard Holter ECG might be a helpful screening tool detecting sleeping disorders in patients with arrhythmias.

P 083
Automatic sleep apnea detection: analysis of apnea distribution with respect to sleep stages, depending on the severity of sleep apnea

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Introduction: The present study investigates the distribution of apnea events with respect to sleep stages, depending on the severity of sleep apnea. The results of this study are based on data recorded in the SIESTA project. A new apnea detection software, which was developed recently for the Somnolyzer24×7, will be introduced.

Method: The apnea detection algorithm is based on 4 polysomnographic signals: oxygen saturation, nasal airflow, movement of the chest wall and of the abdomen. Oxygen saturation is resampled to 4 Hz and peaks of this signal are determined in order to extract intervals of oxygen desaturation. Intervals of decreased airflow are calculated by comparing the signal with a smoothed version of itself and are assigned to two classes: an amplitude decrease of more than 50% and more than 80%. From both the chest and the abdominal movement signals, the same intervals are extracted. The detection of apnea events is accomplished by running through a decision tree resulting either in central, obstructive or mixed apneas or hypopneas. Using the automatically determined R&K stages, all apnea events were further assigned to the sleep stages. For the sake of comparability of measurements, the time with apnea events
during the different sleep stages was determined (in s) and related to the total time of apneas, resulting in percentages. The polysomnograms of 50 subjects (43 males and 7 females, aged 51 ± 10 years) were divided into two groups: 22 subjects with an AHI ≤ 15 (group 1) and 28 subjects with an AHI > 15 (group 2).

Results: Group 1 (mild apnea) had a mean AHI of 6.8. The time with apnea events in stages 1–4 and REM was (in % of the total time of apneas) 26.4, 48.0, 1.0, 0.6 and 24.0%, respectively. The corresponding sleep stages (in % of the total sleep time) were 14.7, 52.6, 8.4, 4.0 and 20.3%, respectively. Group 2 (moderate to severe apnea) had a mean AHI of 31.2. The time with apnea events in stages 1–4 and REM was 23.2, 55.2, 3.3, 0.6, and 17.8%, respectively. The corresponding sleep stages were 19.5, 52.9, 5.8, 2.9 and 18.8%, respectively. Whereas t-tests revealed no significant difference in the distribution of sleep stages between the two groups, a significant difference for the occurrence of sleep apnea was found in stage 3.

Conclusion: Patients with moderate to severe apnea spent significantly more time with apnea in stage 3 than patients with mild apnea, even after correction for the different total time with apnea in both groups. However, our data do not suggest a clear relationship between the distribution of apnea/hypopnea events in the different sleep stages and the severity of the disease.

Acknowledgment: Research supported by Austrian Industrial Research Promotion Fund (Project 806765). The Austrian Research Institute for Artificial Intelligence is supported by the Austrian Federal Ministry of Education, Science and Culture and the Austrian Federal Ministry of Transport, Innovation and Technology.

P 084
The Long-term Effect of Compliance of Nasal Continuous Positive Airway Pressure on Sleep Apnea Hypopnea Syndrome
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Objective: To evaluate the long-term effect of nCPAP compliance on apnea-hypopnea, daytime sleepiness and blood pressure of the SAHS patients.

Methods: 20 compliant patients, 20 non-compliant patients and 28 untreated patients were re-examined, which included polysomnography (PSG), blood pressure before and after sleep, body mass index (BMI) and Epworth sleepiness scale (ESS).

Results: The AHI of the compliant cohort significantly declined from 56.6 ± 23.6 events/hour before treatment to 31.8 ± 20.8 events/hour after treatment (p = 0.001). Their LS$_{O2}$ increased from 64.0 ± 14.5% to 77.3 ± 7.6% (p < 0.001). The data of the non-compliant cohort and the untreated cohort mentioned above were worsened. The compliant cohort attained better scores in ESS than either of the untreated one (p < 0.05).

Conclusions: The AHI and LS$_{O2}$ of the compliant cohort were both better than those prior to treatment were. The compliant cohort got better scores in ESS than the untreated group.

P 085
Serum Adiponectin Levels in Adult Male Patients with Obstructive Sleep Apnea Hypopnea Syndrome
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Background: Adiponectin has been found to be associated with the pathogenesis of diabetes, obesity and some cardiovascular diseases, which usually coexist with obstructive sleep apnea hypopnea syndrome (OSAHS). However, association between adiponectin and OSAHS has hardly been reported.

Objectives: To investigate the levels of serum adiponectin in adult male patients with OSAHS.

Methods: Through polysomnography examination, 84 adult male habitual snorers were divided into simple snorers (control group) and OSAHS patients (OSAHS group) who were further divided into mild, moderate and severe OSAHS subgroups based on their apnea hypopnea index (AHI). There was no significant difference in age, body mass index (BMI), fast blood glucose (FBG) and insulin resistance expressed as homeostasis model assessment (HOMA) between the two groups. The serum adiponectin levels was measured by radioimmunoassay.

Results: Serum adiponectin level was significantly lower in OSAHS group than in control group (P < 0.01). Such a decrease in adiponectin level was most significant in moderate and severe degree OSAHS patients. Pearson correlation analysis showed that in OSAHS patients, serum adiponectin level was negatively correlated with BMI, circumferences of waist (WC) and neck (NC), AHI and HOMA, but positively correlated with nadir pulse oxygen saturation (nadirSpO$_2$). After controlling for HOMA, BMI, NC and WC in OSAHS patients, a partial correlation analysis showed adiponectin levels were negatively correlated with AHI but positively correlated with nadirSpO$_2$. Multiple logistic regression analysis indicated that adiponectin was independently associated with OSAHS.

Conclusions: Serum adiponectin levels were significantly lower in OSAHS patients than in simple snorers. OSAHS may cause decrease in serum adiponectin level.
Vascular endothelial function change in elderly Chinese patients with obstructive sleep apnea and its association with coronary heart disease

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Objective: To investigate the function of vascular endothelial cells (EC) and the plasma levels of nitric oxide (NO) and endothelin (ET) in elderly Chinese patients with obstructive sleep apnea hypopnea syndrome (OSAHS) and its association with coronary heart disease (CHD).

Methods: Elderly simple snorers (n=31) with neither OSAHS nor CHD were randomly selected as the control group; 45 elderly patients with moderate or severe degree of OSAHS were recruited as the OSAHS group, which were further divided into two subgroups, CHD subgroup (16 patients) and non-CHD subgroup (29 patients). The changes of plasma concentrations of NO and ET were compared between the two subgroups.

Results: Compared with the control group, in the OSAHS group there was a significantly lower NO level (27.7 ± 9.2 μmol/L vs 61.9 ± 13.5 μmol/L, P < 0.01), higher ET level (58.1 ± 14.2 ng/ml vs 34.8 ± 8.2 ng/ml, P < 0.01), and lower NO/ET ratio (0.47 ± 0.18 vs 1.72 ± 0.97, P < 0.01). The incidence of CHD in the OSAHS group was 35.6%. Comparison between the control group and non-CHD OSAHS subgroup showed that the decreased NO level (35.5 ± 9.4 μmol/L), increased ET level (47.5 ± 11.1 ng/ml) and declined the NO/ET ratio (0.75 ± 0.13) in non-CHD subgroup were statistically significant (P < 0.05). This difference was more significant between the control group and CHD OSAHS subgroup (P < 0.01). Comparison between the two OSAHS subgroups indicated that there was a significantly lower NO level, higher ET level and more declined NO/ET ratio in those with OSAHS and CHD than in the OSAHS without CHD subgroup (all P < 0.05).

Conclusion: Vascular endothelial function was significantly impaired in elderly Chinese patients with OSAHS, especially in those with both OSAHS and CHD. Dysfunction of the vascular EC may be one of the causes of CHD in OSAHS patients.

Restless Legs Syndrome

Validity of the Essential Criteria and Additional Clinical Features for the Diagnosis of Restless Legs Syndrome

Beneš H. (Schwerin, Germany), Kohen R. (Nuremberg, Germany)

Introduction: Diagnosis of RLS is mainly based on the four essential diagnostic criteria of the International Restless Legs Study Group (IRLSSG). In addition, 3 supportive and 3 associated features should be considered (Allen et al., Sleep Medicine 2003; 4:101–129). No empirical data are currently available which investigate the validity of those diagnostic criteria.

Methods: We report on findings from a diagnostic study. A cohort of all patients with sleep disturbances from our sleep lab was interviewed on the telephone. We asked the patients how frequent the essential symptoms were present (5 to 7 days per week or 1 to 4 days per week, or never) or if additional clinical features were definitely or questionably present. Sensitivity and specificity of each criterion were calculated using the final primary diagnosis for sleep disturbances of two independent neurologists as validation criterion.

Results: Of 265 patients in the cohort with sleep disturbances as reason for the diagnostic assessment in the sleep lab, N=179 (67.2%) participated in the interview (females: 64.8%, mean age: 56 years) N=86 patients had a final diagnosis of RLS and n=93 patients had any other sleep-related disorder.

<table>
<thead>
<tr>
<th>Diagnostic criteria</th>
<th>Present at 5 to 7 days</th>
<th>Present at 1 to 7 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential criteria</td>
<td>Sensitivity Specificity</td>
<td>Sensitivity Specificity</td>
</tr>
<tr>
<td>Urge to move</td>
<td>81.3% 81.7%</td>
<td>95.3% 70.9%</td>
</tr>
<tr>
<td>Unpleasant sensations</td>
<td>73.2% 82.7%</td>
<td>91.8% 68.8%</td>
</tr>
<tr>
<td>Onset at rest</td>
<td>82.5% 87.0%</td>
<td>97.6% 74.1%</td>
</tr>
<tr>
<td>Relief when moving</td>
<td>66.2% 86.0%</td>
<td>94.1% 68.8%</td>
</tr>
<tr>
<td>Worsening in the evening</td>
<td>83.7% 80.6%</td>
<td>96.5% 72.0%</td>
</tr>
<tr>
<td>Additional features</td>
<td>Definite Questionable</td>
<td></td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>87.2% 17.2%</td>
<td>91.8% 13.9%</td>
</tr>
<tr>
<td>Family history of RLS</td>
<td>38.3% 89.2%</td>
<td>46.5% 83.8%</td>
</tr>
<tr>
<td>Response to dopaminergics</td>
<td>94.1% 94.6%</td>
<td>97.6% 92.4%</td>
</tr>
<tr>
<td>Period limb movement</td>
<td>84.8% 90.3%</td>
<td>93.0% 79.5%</td>
</tr>
<tr>
<td>Neurological assessment</td>
<td>83.7% 98.9%</td>
<td>100% 84.9%</td>
</tr>
</tbody>
</table>

Conclusions: To increase sensitivity of the essential criteria, frequency of occurrence should not be restricted. However, specificity of the essential criteria is poor under such conditions. False positive diagnoses (RLS mimicks) will be frequent. Both specificity and sensitivity can be remarkably increased by inclusion of specific additional features for RLS diagnosis. Sleep disturbances are not specific for RLS and family history occurs in less than half of the population. We recommend that for diagnosis of RLS at least one of the additional features except sleep disturbances should be definitely present to exclude RLS mimicks, and to increase sensitivity.
P 088
The Restless Legs Syndrome Diagnostic Index (RLS-DI): Validation of an Algorithm for the Diagnosis of the Restless Legs Syndrome (RLS)

Beneš H. (Schwerin, Germany), Muchalski T. (Magdeburg, Germany), Kaulfuß L. (Rostock, Germany), Kohmen R. (Nuremberg, Germany)

Introduction: Diagnosis of RLS is mainly based on the 4 essential diagnostic criteria of the International Restless Legs Study Group (IRLSSG). Recently, “mimicks of RLS” have identified the problem of a suboptimal specificity of the essential criteria. With the RLS-DI, a diagnostic algorithm is provided which determines the probability of a RLS diagnosis. The RLS-DI has 10 items which comprise the essential criteria (5 items), and sleep disturbances, family history of RLS, polysomnographic findings, response to dopaminergic treatment, and neurological expert diagnoses to identify RLS or to exclude other causes of RLS symptoms. In an innovative approach to increase specificity, the RLS-DI gives negative weights to items if a cardinal RLS symptom is not present. The RLS-DI total score therefore ranges between -25 (no RLS) and 20 (definite RLS). Data from a first validation study of the RLS-DI are presented.

Methods: From the cohort of all patients who were evaluated in our sleep laboratory during the years 2003 and 2004, patients with sleep disorders for any reason were invited to participate in a telephone interview. During the interview, the RLS-DI and the IRLS severity scale and other scales were completed; patients were asked for the status prior to any specific therapy. Sensitivity, specificity, and Receiver Operating Characteristic (ROCs) were calculated using the final primary diagnosis for sleep disturbances of two independent neurologists as validation criterion.

Results: Of 265 patients in the cohort with sleep disturbances as reason for the diagnostic assessment in the sleep lab, N = 179 (67.2%) participated in the interview (females: 64.8%, mean age: 56 years). N = 86 patients had a final diagnosis of RLS and n = 93 patients had any other sleep-related disease (OTH: insomnia (n = 69), neurological (n = 13), psychiatric disorders (n = 9), or orthopedic disease (n = 2). The inter-rater reliability with regard to diagnosis of the two experts was kappa = 0.93. Both groups differed in the RLS-DI (+15.9 ± 4.5 vs. -8.4 ± 8.9, p < .0001) and in the IRLS total score (30.1 ± 7.9 vs. 7.2 ± 12.1, p < .0001). Using a cut-off of 10 RLS-DI score points for probable RLS as confirmed by ROC analysis (AUC = 98.5%), sensitivity of the RLS-DI was 94.2% and its specificity was 95.7%. A portion of 95.0% of all patients could be correctly classified by the RLS-DI. In 4 false positives OTH patients (4.5%), secondary or intermittent RLS was reported as comorbidity. In 5 false negative RLS patients (5.8%), intermittent RLS was found in the medical history but patients did not remember this condition due to impaired cognitive function.

Conclusion: The RLS-DI is a valid and easy to use tool to confirm or exclude the diagnosis of RLS. In addition to the essential diagnostic criteria at least one of the features family history, polysomnographic findings, dopaminergic response, or neurological diagnoses should be definitely present to exclude RLS mimicks.

P 089
Transdermal Lisuride in patients with idiopathic Restless Legs Syndrome: Results from a placebo-controlled, double-blind, randomized, multicenter, 12-week dose-finding study

Beneš H. (Schwerin, Germany) on behalf of the TULIR study group

Introduction: Restless Legs Syndrome (RLS) patients suffer from symptoms not only at bedtime but also with variable circadian patterns. Transdermal application forms of dopamine agonists are expected to lead to a stable plasma concentration of the active drug which could ease treatment of RLS patients with daytime symptoms and avoid side effects of intermittent oral dopaminergic therapies.

Methods: This was a multicenter, randomized, double-blind, placebo-controlled dose-finding study with 12-week treatment in four treatment arms (Lisuride TTS patches: 10, 20, 40 cm²; 2, 5, 10 mg Lisuride, placebo). Patches (4×10 cm²) were applied every other morning, i.e. over 48 hours. Efficacy was assessed with the IRLS, the RLS-6 scales, CGI, SF-A quality of sleep and QoL-RLS quality of life questionnaire. Statistical analysis compared each active treatment to placebo in a closed test procedure, using Least Squares (LS) means from an ANCOVA with treatment as factor and baseline measures as covariate.

Results: 210 patients (70% females, age 60 ± 11 years, 4 uremic and 206 idiopathic RLS) were randomized. The RLS diagnostic index was 16.5 points (range 11 to 20) on average indicating that all patients suffered from RLS. The IRLS total score (primary endpoint) improved dependent on dose between baseline (mean:28.8) and endpoint as follows:

Placebo: −9.5, 10 cm²: −14.7, 20 cm²: −18.4, 40 cm²: −18.9; all active doses of Lisuride TTS were superior to placebo (p = .0148 for 10 cm², p < .0001 for 20 and 40 cm²). Responder rates (50% improvement from baseline) were: 26.9%, 43.4%, 62.3%, 66.0% (placebo to 40 cm²). In the CGI item 2 “change of condition”, rates of patients who improved “much” or “very much” were 44.2%, 58.5%, 66.0%, 80.0%. In the additional efficacy measures and in the QoL-RLS, mainly the two higher doses of Lisuride TTS were superior to placebo. Tiredness during the day (RLS-6) and sleep were improved by all doses of lisuride TTS (RLS-6 scales).
Most frequent drug-related adverse events (AEs) were local skin reactions, mainly pruritus and erythema, and gastrointestinal symptoms, mainly nausea. Orthostatic hypotension was the only one serious adverse event (20 cm²). In 54 patients (25.7%), AEs were associated with premature discontinuation from the trial (15.1%, 20.8%, 33.3%, 34.0%). Again, skin reaction were the most frequent AEs in this context.

**Conclusions:** Transdermal lisuride was effective in all doses investigated in the treatment of RLS symptoms. The dose-response curves in different efficacy measures show that 10 cm² (2.5mg lisuride) and 20 cm² (5 mg lisuride) might be the preferred doses for RLS therapy since the highest 40 cm² dose did not add much to the efficacy of the 20 cm² dose. Skin reactions were the most frequent AEs to be analyzed in forthcoming trials. This is the first large placebo-controlled study to demonstrate that continuous dopaminergic stimulation can be achieved over 48 hours in a dose-dependent way with transdermal lisuride.

**P 090**
**Relationship of Patient-Reported Restless Legs Syndrome (RLS) Rating Scale Scores With Visual Analogue Scale Measures of RLS**

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**Aims:** RLS severity has been evaluated in clinical trials with the International RLS Rating Scale (RLSRS) as well as with visual analogue scales (VASs). Baseline data from 344 patients diagnosed with idiopathic RLS using the Clinical RLS criteria of the International RLS Study Group (IRLSSG) in a randomized, double-blind, placebo-controlled, clinical trial were analyzed to determine the correlation of these 2 instruments.

**Methods:** The following measures were collected during the baseline period of this clinical trial: RLSRS is a 10-item scale rated by the patient covering the RLS severity of the past week on 5 levels (none to severe) with a maximum sum score of 40; in parallel patients rated their RLS severity while getting to sleep, in the course of the night, in the course of the day and satisfaction with sleep with VAS (a 100-mm line where the patient rates RLS severity over the past week with a hash mark [0=not present, 100=severe; and 0=very satisfied, 100=very dissatisfied for the latter]). Higher scores on all scales indicate worse RLS severity.

**Results:** Overall baseline means for this RLS study population were RLSRS 23.5 ± 5.1, VAS ‘RLS severity while getting to sleep’ 64.7 ± 26.6, VAS ‘RLS severity in the course of the night’ 61.0 ± 28.0, VAS ‘RLS severity in the course of the day’ 31.2 ± 23.7, and VAS ‘satisfaction with sleep’ 68.3 ± 24.1. Moderate, severe, and very severe RLS was reported in 32.8%, 57.5%, and 9.6% of patients utilizing the RLS rating scale intervals, corresponding to medians in VAS RLS ‘severity while getting to sleep’ of 52, 79, and 92 mm; VAS ‘RLS severity in the course of the night’ of 50, 73, 91 mm; VAS ‘RLS severity in the course of the day’ of 24, 30, 45 mm; and VAS ‘satisfaction with sleep’ of 52, 79, 94 mm. Spearman’s rank correlation coefficients (r-values) between these measures were as follows:

<table>
<thead>
<tr>
<th>RLSRS</th>
<th>VAS severity ‘while getting to sleep’</th>
<th>VAS severity ‘in course of the night’</th>
<th>VAS severity ‘in course of the day’</th>
<th>VAS ‘satisfaction with sleep’</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.52</td>
<td>0.51</td>
<td>0.23</td>
<td>0.61</td>
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</table>

High correlation coefficients (>0.50) were also found for the VAS ‘satisfaction with sleep’ and the RLSRS items ‘tiredness during the day’ and ‘sleep disturbances due to RLS’.

**Conclusions:** About 2/3 of this RLS study population had severe to very severe RLS at baseline. RLS severity as measured by the RLS rating scale was highly correlated with the RLS severity as measured by VASs. The baseline RLSRS scores are most well correlated (r=0.61) to the VAS ‘satisfaction with sleep’. Better scores in the VAS ‘satisfaction with sleep’ are highly correlated with better scores in those items from the RLS rating scale dealing with sleep, namely ‘tiredness during the day’ and ‘sleep disturbance due to RLS’.

**P 091**
**The Hormonal Hypothesis of RLS Revisited-Prevalence of RLS in Transsexuals**

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The hypothesis that RLS is associated with altered levels of hormones receives its major support by the well-documented finding that there is a markedly high incidence of RLS in pregnant women. Up to one third of them experience RLS mostly during the last trimester of pregnancy. During pregnancy prolactin, progesterone and estrogens are at high levels peaking during the third trimester. To explore whether high levels of estrogens are associated with RLS we examined the incidence of RLS in transsexual patients who are treated with high doses of either testosterone or estrogens. Questionnaires including the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS), as well as questions regarding the four cardinal symptoms of RLS were mailed to 288 transsexual patients registered within the last 5 years at the outpatient clinic for endocrinology at the Max Planck Institute of Psychiatry. The four cardinal symptoms of RLS are (1) an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs, (2) the urge to move or
unpleasant sensations begin or worsen during periods of rest or inactivity, (3) worsening of symptoms at rest with at least partial and temporary relief by activity, and (4) worsening of symptoms in the evening or night. From the 288 questionnaires mailed 102 could not be delivered and were returned. To date, 77 persons replied (41% of 186). Sixty-nine persons did take estrogens (n = 29) or testosterone (n = 40). Twenty-four percent (7 of 29) of persons taking estrogens had all four symptoms of RLS, while the corresponding rate was 10% (4 of 40) for persons taking testosterone.

Conclusions: These preliminary data point to a high incidence of RLS in transsexual patients who are taking high doses of estrogens. This supports the hypothesis that estrogens may play a role in the pathophysiology of RLS.

P 092
On the development of the “Structured Interview for Diagnosis of Augmentation during RLS treatment” (RLS-SIDA): First experiences

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Introduction: Augmentation (AUG) reflects an overall increase in symptoms severity as a result of long-term dopaminergic treatment. The clinical features of AUG are: (A) earlier onset of symptoms during the day, (B) increase in symptom severity, (C) shorter latency to symptoms when at rest, (D) spreading from legs to upper limbs, compared to no or stable previous treatment. No standardized instrument is currently available to diagnose the presence or exclusion of AUG. Here we report on the development of the RLS-SIDA and present first empirical data.

Methods: By using the NIH criteria for AUG (Allen et al., Sleep Medicine, 2003) and the authors’ clinical experience, specific questions were developed that allowed determination of the four key diagnostic features of AUG. The RLS-SIDA was administered by two independent trained raters to each patient in whom the treating physician suspected possible augmentation. The outcome of the interview was compared to the diagnosis on augmentation of an expert with extensive experiences with AUG. RLS patients who were on current dopaminergic treatment were included in 2 centers in Austria and Spain.

Results: The RLS-SIDA was applied to 24 patients (69.6% females, age 59 ± 16 years). According to the expert, AUG was present 13 patients (54.2%). With 2 exceptions, AUG was correctly diagnosed by the RLS-SIDA. One patient was falsely positive or falsely negative diagnosed by the interviewers. Sensitivity was 92.3% and specificity was 90.9% in this small sample. Inter-rater reliability for the final diagnosis was kappa = .916 (p < .001), it was even higher in most single items of the RLS-SIDA.

Conclusions: The RLS-SIDA is promising to become a sensitive, specific, and reliable instrument for diagnosing augmentation during drug treatment of RLS. Development and validation are still ongoing.

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P 093
Prevalence of restless legs syndrome in patients treated with neuroleptics

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Aim: The aim of this study was to assess whether there is a relationship between intake of neuroleptic drugs and incidence of the restless legs syndrome (RLS).

Methods: An original questionnaire based upon diagnostic criteria of the RLS created by International Restless Legs Syndrome Study Group was used in this study. The questionnaire contained also questions about supportive clinical features of RLS, demographic features of the patients and their health status. The questionnaires were filled in by the patients during their stay in the Department of Mental Disorders. The data about the patients’ diagnosis and therapy were then collected. Patients participated in the study by their own will.

Results: We have examined 111 patients from Department of Mental Disorders of Medical University of Gdansk (71 females and 40 males). The mean age of the examined group was 44.9 years. Most patients were suffering from following diseases: schizophrenia, depression, anxiety disorders and bipolar disorder. Forty-eight patients (43.2%) were treated with neuroleptics. In the group of patients taking neuroleptics we have found 16 subjects with symptoms of the restless legs syndrome (33.3%). The incidence of restless legs syndrome in the group of patients not treated with neuroleptics was lower—we have found 12 patients with symptoms of RLS in this group (19%).

Conclusions: The incidence of symptoms of restless legs syndrome in the group of patients taking neuroleptics was higher than in the population of patients treated with another drugs. Establishing a correlation between intake of specific neuroleptics and incidence of RLS needs further studies with larger groups of patients.
Rotigotine patch efficacy and safety in the treatment of moderate to severe idiopathic restless legs syndrome—results from a multi-national double-blind placebo-controlled multi-center dose-finding study

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Introduction: Patch administration of dopamine agonists is a promising innovative approach for the treatment of Parkinson’s disease and restless legs syndrome (RLS). Continuous drug delivery and stable plasma levels are expected to enable symptom relief for a 24-hour period and avoid tolerability problems which are common for oral application of dopamine agonists.

Methods: A double-blind, six-arm, parallel group, randomized, placebo-controlled dose-finding study with the dopamine agonist rotigotine was performed at 34 centers in Austria, Germany, and Spain. Patients were treated with 1.125 mg, 2.25 mg, 4.5 mg, 6.75 mg, or 9 mg rotigotine/day, or placebo in a 7 week trial. Primary efficacy measure was the change in the total score of the IRLS severity scale. As secondary efficacy measures, the Clinical Global Impressions (CGI) and the RLS-6 severity ratings were administered and quality of life were assessed with the QoL-RLS.

Results: Of 371 enrolled patients with moderate to severe idiopathic RLS, 340 (age 58 ± 10 years, 70% females) were randomized. Baseline IRLS total score was 27.9 ± 6.0. The adjusted mean changes from baseline to week 6 in the IRLS total score were as follows: 1.125 mg, −10.6; 2.25 mg, −15.1; 4.5 mg, −15.7; 6.75 mg, −17.5; 9 mg, −14.8, for placebo −9.2 points. The treatment difference (rotigotine-placebo) was statistically significantly different (ANCOVA) for all rotigotine doses, except the 1.125 mg dose with the largest difference of 8.3 points between 6.75 mg rotigotine and placebo. Clinically relevant improvement of more than 6 points in the IRLS was observed in 70% (1.125 mg) to 88% (4.5 mg), compared to 62% of the placebo-treated patients.

Restless Legs Syndrome and Periodic Limb Movements during Sleep among Japanese Industrial Workers

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Introduction: Restless legs syndrome (RLS) is clinically diagnosed when the symptom of a patient fulfils the all four diagnostic criteria items of NIH/IRLSSG. On the other hand, diagnosis of periodic limb movement during sleep (PLMS) require sleep investigation. However, most of the previous epidemiological studies in Japan had such limitations as using a questionnaire without any validation, few systematic study with face-to-face interview, and/or small sample size for sleep investigation. The aim of the study was (1) to validate the questionnaire for epidemiological study of RLS and PLMS, and (2) to reveal the prevalence of RLS and PLMS among the Japanese industrial workers from the result of both face to face interview by the specialists in neurology/sleep medicine and simple leg activity monitoring device.

Methods: One hundred and forty one industrial workers (all male, age 44.6 SD 8.4 years) who joined the Kyoto Sleep and Health Cohort Study (KSHS) were included in the study. A minimum question set was recommended for the epidemiological study at the NIH workshop was translated into Japanese and a single question about PLMS was created. Questionnaire was
answered by each subject before the face-to-face interview. RLS was diagnosed when all four NIH/IRLSSG criteria were met. Questionnaire answer was compared with the clinical diagnosis. PLMS were measured with a leg activity monitoring device (PAM-RL) for four consecutive nights (2 nights on the right, 2 nights on the left). Actigraphy was used to estimate sleep period. PLMS was diagnosed when the mean periodic limb movement index (PLMI/hour) of four night recordings was more than 5 per hour.

Results: Twelve subjects (8.5%) were clinically diagnosed as RLS and 25 subjects (18.4%) had PLMI of more than five. 14 subjects had positive questionnaire diagnosis of RLS while 4 subjects with clinical diagnosis of RLS had negative questionnaire diagnosis. Sensitivity of the questionnaire was 66.7%. Among the subjects with positive questionnaire diagnosis of RLS, 5 (35.7%) had misunderstood the muscle cramp of the leg as sensory discomfort of RLS. Mean PLMI of the subjects with PLMI of more than 5 was 15.3 SD 14.3/hour. 12 subjects had positive questionnaire diagnosis of PLMS, and the sensitivity of the single question was 32.0%. Among the subjects with PLMI of more than five, only one of them complained sleep disturbance due to PLMS.

Conclusion: Prevalence of RLS in our population was higher than the previous Japanese reports and quite compatible with that of Western population. PLMD was only seen in less than 1% of the subjects, suggesting that PLMD is less severe among Japanese population. Judged from the low screening sensitivity with questionnaire, this kind of epidemiological study may underestimate the prevalence of RLS and PLMS. This on-going study may provide further information on what kind of modification would be possible for the improvement of the questionnaire.

P 096
Prevalence of Restless Legs Syndrome in urban and rural populations of General Practitioners Patients

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Aim: The aim of the study was to compare the prevalence of Restless Legs Syndrome (RLS) in populations of patients of General Practitioners in urban and countryside areas of Northern Poland. We wanted to check whether social and cultural factors influence the prevalence of RLS.

Methods: We have used an original questionnaire based upon the International Restless Legs Syndrome Study Group diagnostic criteria containing also questions about demographic features and general health condition of the subjects. RLS trained interviewers were taking structuralised medical interviews with patients of primary care settings in Gdansk and rural areas of Northern Poland helping them to answer the questions of the questionnaire.

Results: We have examined 2155 subjects (947 subjects in urban area and 1208 subjects in rural areas). The sex and age structure of both groups were similar (421 M/526 F and 616F/592M and mean age was 45.4 and 43.4 years respectively). The prevalence of RLS in urban area was 20.2% and in the rural area 15.1%. The examined populations differed in other aspects such as prevalence of coronary heart disease (14.9% vs 12.1%), hypertension (25.2% vs 20.4%), kidney disease (7.4% vs 5.1%), diabetes mellitus (7.7% vs 4.2%), overusage of caffeine (63% vs 54.8%), nicotinism (28.8% vs 34.3%), insomnia (39.1% vs 28.8%) and daytime sleepiness (36.3% vs 37.1%).

Conclusion: The coincidence of difference in prevalence of RLS in urban and rural population with differences of prevalence of other conditions suggests that RLS rather is not dependant on the social condition of the subjects. Further studies on the aetiology of RLS should still be focused on the biological and not social factors.

P 097
The prevalence of the Restless Legs Syndrome in the population of patients with connective tissue diseases

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Aim of the study: The aim of this study was to assess the prevalence of the Restless Legs Syndrome (RLS) among the patients with connective tissue disease (CTD) and to correlate the presence of RLS with the type of CTD and its course.

Methods: An original questionnaire based upon diagnostic criteria of the RLS created by International Restless Legs Syndrome Study Group was used in this study. The questionnaire contained questions about supportive clinical features of RLS, demographic features of the patients and the co-morbid diseases. RLS-trained interviewer was filling in the questionnaire while taking a structuralized medical history from the patients of Connective Tissue Diseases Out-patient Department, Medical University of Gdansk, Poland. The questionnaires were anonymous.

Results: The questionnaires were filled in for 110 patient (103 F and 7 M). The mean age of the examined group was
50.06 years. RLS was found in 42 patients (38.2%). The RLS-positive patients were suffering from systemic lupus erythematosus (SLE) (61.9%), Sjogren’s syndrome (11.9%), sclerodermy (7.1%) and rheumatoid arthritis (4.7%). RLS was present in 33.3% of patients with CTD and nephropathy and in 47.8% of patients with CTD and anaemia.

**Conclusion:** We have found high prevalence of RLS in the population of patients with CTD. It is most common among patients with SLE. There is also a coincidence of RLS and nephropathy and anaemia that suggest that RLS is rather secondary to the complications of CTD than to the CTD itself.

### P 098

**The prevalence of Restless Legs Syndrome in the population of patients with symptoms of depression**

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**Aim:** The aim of the study was to assess the prevalence of Restless Legs Syndrome (RLS) among patients with depressive symptoms, especially those who are not treated because of depression.

**Methods:** A population of patients of a selected Primary Care Setting was examined in this study. We have used Beck’s Depression Index for screening the population for symptoms of depression. Screening for RLS was performed with an original questionnaire based upon diagnostic criteria of International RLS Study Group. We have also added some questions whether the depression is diagnosed and treated.

**Results:** We have screened 311 subjects (104M and 207F). The mean age of the group was 43.7 years. Symptoms of depression (according to BDI) were found in 110 subjects (35.3%). RLS was found in 66 subjects (21.2%). We have divided the examined population into three groups: subjects without symptoms of depression (group I, n = 196), subjects treated for depression (group II, n = 20) and non-treated subjects with symptoms of depression (group III, n = 95). The prevalence of RLS in each of the group was as follows: group I-17.8%; group II- 20%; group III-27.3%.

**Conclusion:** Undiagnosed depression is a common problem in the primary care. The highest prevalence of RLS was in the group of untreated depression. The fact of high prevalence of RLS in this population should be consider in any epidemiologic study on RLS performed in the primary care settings.
diagnosis of RLS can be established during the initial diagnostic process, especially, if alternate causes might explain the motor and sensory symptoms (RLS mimics). The L-DOPA test is an approach which can be applied easily even by physicians who are not experts in neurology in general and in RLS in particular.

P 100
Clinical characteristics of restless legs syndrome in patients with Parkinson’s disease

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Aims: Some epidemiological studies have showed that the prevalence of restless legs syndrome (RLS) is clearly higher in patients with Parkinson’s disease (PD) than general population. However, either background factor causative for the occurrence of RLS in PD patients group and clinical characteristics of the disorder has not been well elucidated. In order to clarify these issues, we compared the clinical backgrounds, severity of RLS symptom and treatment outcome between PD patients with RLS (pRLS) and idiopathic RLS (iRLS).

Methods: Thirteen consecutive pRLS patients (6male and 7female) with 65.5 ± 5.5 years of mean age and 22 iRLS patients (8 male and 14 female) with 59.5 ± 14.3 years of mean age who visited our outpatient clinic seeking for the treatment of RLS were enrolled in this study. A comparison on the variables including age, gender distribution, onset age and length of RLS morbidity, family history of RLS and serum values of both Fe and ferritin was made between the two groups. Pittsburgh Sleep Quality Index (PSQI) indicating the severity of sleep disturbance and the International Restless Legs Syndrome Study Group (IRLSSG) severity scale of RLS and polysomnographic variables before treatment were also compared. Moreover, daily dosage of dopaminergic agents (DA) and clonazepam (CLZ), and the treatment response of the drugs for RLS were compared between the two groups.

Results: Among pRLS patients, mean length from the onset of PD symptom to the occurrence of RLS symptoms was 3.4 ± 3.2 years. Age at onset of RLS was significantly higher (p < 0.05) and length of RLS morbidity at the investigation was significantly shorter (p < 0.05) in the pRLS patients than iRLS patients. The rate of the patients with family history of RLS was significantly higher in iRLS than pRLS (p < 0.05). No difference in the scores of PSQI, IRLSSG severity scale and parameters of sleep architecture between the two groups, while periodic limb movements index (PLMI) was remarkably lower in pRLS. As for the treatment outcome, the scores of IRLSSG severity scale was quite similar between the two groups despite the dose of DA and CLZ being higher in the pRLS group.

Conclusion: Our results revealed that pathological mechanism of RLS is not the same between the two groups. Judging from the lack of family history, the elderly onset and the rapid progression of the symptom after the onset of the disorder, it could be plausible that pRLS occurs on the basis of both PD and physiological aging. Poor treatment response to DA in the pRLS group might derive from the degeneration of dopaminergic system due to PD, and the finding strongly emphasizes the necessity for developing new therapeutic strategy in this RLS patients group.

P 101
Augmentation and lack of efficacy with dopaminergic treatment in patients with RLS. Double-blind comparison between cabergoline and L-dopa in the treatment of patients with severe Restless Legs Syndrome

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Introduction: From clinical experience, open-label trials and retrospective analyses, augmentation is a serious complication of treatment with dopaminergic drugs in Restless Legs Syndromes (RLS) patients. In addition, the rate of non-responders to such treatment has not yet been prospectively determined in previous RLS drug trials. We report on the risk of augmentation and lack or loss of efficacy as assessed in the first large-scale double-blind, randomized study to compare two active dopaminergic therapies for RLS, the dopamine agonist cabergoline (CAB) and L-dopa/benserazide (LEV).

Methods: Patients with idiopathic RLS were treated with fixed daily doses of 2 mg CAB or 200 mg LEV; in the event of insufficient efficacy after six weeks, dose was increased to 3 mg CAB or 300 mg LEV. Study duration was 30 weeks. Augmentation and lack/loss of efficacy was assessed by the investigators. No standardized scale for the evaluation of augmentation is currently available. We analyzed (a) the rate of patients who discontinued from the trial to either event (primary efficacy outcome measure) and (b) the rate of patients in whom any clinically relevant sign of either event occurred during the 30-week trial.

Results: 361 of 418 screened patients (age 58 ± 12 years, 71% females) were randomized and treated (CAB: n = 178; LEV: n = 183) in 51 centers of 4 European countries. Baseline IRLS total score was 25.7 ± 6.8 which corresponds to “severe” intensity of RLS on average. Dose increase was more frequently required in LEV patients (49.4%) vs. CAB (24.1%, p < .001).

(a) During the 30 weeks treatment period, more patients of the LEV group (24.0%) than of the CAB group
(11.9%) discontinued due to lack/loss of efficacy or augmentation (p=.0029, log-rank test, intention-to-treat population). Discontinuation from the trial was caused in 9.8% (LEV) vs. 4.0% (CAB) by augmentation (p=.0412) and in 14.2% (LEV) vs. 7.9% (CAB) by lack of efficacy (p=.0290).

(b) Any signs of augmentation or lack/loss of efficacy causing discontinuation from the trial or being tolerated by the patients were reported in 38.8% (LEV) vs. 19.2% (CAB) of the patients (p=.0003). Any symptoms of augmentation occurred in 14.2% (LEV) vs. 5.6% (CAB, p=.0104) and any insufficient efficacy in 24.6% (LEV) vs. 13.6% (CAB, p=.0100).

Conclusions: This first large-scale active controlled study in RLS showed superior efficacy of cabergoline versus L-dopa after a 30-week therapy. Treatment complications due to loss of efficacy or augmentation were less frequent under cabergoline than under L-dopa. For L-dopa, the rate of 14% of patients with augmentation over a 30-week period under double-blind conditions was surprisingly low compared to data from previous open-label or retrospective trials. However, the limitation of daily dose to 300 mg L-dopa might have avoided augmentation in favor of a high rate of patients experiencing lack or loss of efficacy.

P 102
Restless Legs Syndrome and body temperature

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The prevalence rate of the Restless Legs Syndrome (RLS) has been estimated to be 5–15%; the known cases of RLS suggest a genetic predisposition.

Ten Estonian male patients aged 21–66 years with severe RLS on the basis of the RLS Rating Scale and ten same-aged male subjects without sleep disorders.

Digital PSG recording systems (SomnoStarPro) were used including standard PSG with respiratory and snoring thermistors and finger pulse oxymeter, EKG, EMGs of both anterior tibial muscles and temperature thermistors (Jaeger). We compared the polysomnograms with body temperature of RLS patients and normal subjects.

The mean sleep PLM index was 25 ± 15, and the mean wake PLM index was 50 ± 28 in RLS patients. RLS patients had a significantly lower body temperature, but the maximum drop in the body temperature was not considerable by comparison with the normal subjects. RLS patients revealed significantly less total sleep time and slow-wave sleep, longer sleep latencies, and higher frequency of waking by comparison with the normal subjects.

Periodic Limb Movements

P 103
Actigraphic detection of periodic leg movements: further validation studies

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Aims: The aim of our study was to compare the parameters of actigraphic detection of periodic leg movements (PLM) in two different positions: round the ankle and at the base of the big toe.

Methods: We simultaneously performed polysomnographic (PSG) (Schwarzer BrainLab 3.3) and actigraphic recordings (Cambridge Actiwatch AW-64) in 19 patients (3 women, mean age of the group was 51.2 ± 12.1 years) for 21 nights. Actigraphs were placed round ankles and at the dorsal base of big toes on both legs. We extended the maximum duration criterion of leg movement to 9s in accordance with manufacturers’ recommendation, otherwise standard PLM scoring criteria were applied for both detection methods (polysomnography and actigraphy). Absolute numbers of both periodic and total leg movements were used for comparison between actigraphy and PSG. Periodic leg movement index (PLMI) was computed as ratio of total periodic leg movements and total sleep time for PSG. Time in bed had to be used for actigraphs. Specificity and other related parameters were computed against reference PSG results regarding the PLMI value for both position of actigraph. Threshold of PLMI = 5 was used as cut-off for positivity in PSG and actigraphic recordings from the base of the toes, PLMI = 3 at ankles. Number of apneas and hypopnoeas per hour of sleep (AHI) was recorded by PSG to estimate the influence on results of actigraph.

Results: We have proven significant correlation of all parameters when comparing actigraphy at either position to the polysomnography. Closer correlations were observed at toes (rho = 0.64 vs. 0.81 for PLMI), however the PLMI value obtained by the actigraphy at toes was significantly higher (Sign test p = 0.0005). Comparing ankle vs. toe actigraphic placement yielded sensitivity 77.8% vs. 100%, specificity 91.7% vs. 75%, negative predictive value 84.6% vs. 100%, positive predictive value 87.5% vs. 75% and total accuracy in both 85.7%. Using multiple model regression, the best model of relationship between values obtained from actigraphy and PSG seems to be linear and best predictor is PLMI from toes (R = 0.89615 variance explained: 80.308%). Multiple regression has proven marginally significant effect of AHI on PLMI actigraphy-PSG relationship only at ankles (p = 0.0157).

Conclusions: Comparing to two actigraphic measurements, the first one from the base of big toe is less specific, but more sensitive. It has higher negative predictive value
and better correlates with polysomnographic results than that from ankles. Results from actigraphy also seem to be less affected by presence of respiratory events. These results suggest good validity of actigraphic PLM evaluation at the base of big toe using AW-64 devices. Since this method is faster, cheaper and enables longer recordings as compared to PSG, it seems suitable for screening purposes in both clinical and research usage.

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P 104
Validation of Emfit sensor in detecting periodic movements

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Aims: The standard method for detecting periodic leg movements is the anterior tibialis EMG (AT-EMG). The static-charge-sensitive bed (SCSB, 74×180 cm) has been shown to be suitable for detecting periodic movement activity and a good alternative to AT-EMG recordings. Emfit (ElectroMechanical Film) is elastic, permanently charged electret film that converts mechanical stress into proportionate electrical energy. Emfit sensor’s dimensions are 32×62 cm and it is placed under the patient’s back under the sheet to detect respiratory movements. We compared the performance of the Emfit with AT-EMG and the SCSB as references in detecting periodic movements.

Methods: 16 polysomnograms with AT-PLM Index ≥5/h were analysed. Periodic movements in AT-EMG, SCSB and Emfit were scored separately.

Results: Periodic movement indexes were divided into three severity categories. In 12 out of 16 cases indexes were of the same category with all three methods. In two cases Emfit and AT-EMG showed the same severity category and in the rest two cases Emfit agreed with SCSB.

Conclusions: Emfit sensor performed well in detecting periodic movements and grading the severity of movement disorder. In none of the cases Emfit disagreed with both other methods. Interestingly although Emfit is placed under the thoracic area it doesn’t seem to diminish its usefulness in detecting periodic movements.

P 105
Periodic Leg Movement in users of Anabolic Androgenic Steroids: an observational study

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Objective: To evaluated of the sleep pattern and sleep disorders of anabolic androgenic users that pratice resistance exercisers.

Methods: Samples were composed of 41 young males, all of them performing resistance exercise. They were distributed into two groups; a) experimental group: composed by 20 users of AAS aging 26±1 years and b) control group: 21 non-users of AAS aging 26±1 years. Patients were submitted to all-night polysomnography (PGS) register after an adaptation night. For the all-night PSG registers Sonolab, Meditron was used. All data were expressed by mean ± SEM.

Results: The experimental group has shown an increase in the REM sleep latency (102±12,01 vs 74,8±4,2 min; p=0,04) and in the time percentage spent in stage 4 of the sleep (S4) (14,79±1,35 vs 11,29±1,07; p=0,04) and a decrease in the sleep efficiency (84,03±2,64 vs 91,03±1,03 (%); p=0,01). Furthermore, an elevated frequency of periodic leg movements (PLM) in the experimental group was verified (Fisher test p=0,04).

Conclusion: Taking this data together, the use of AAS can be the responsible by the increase in the time percentage spent in S4, with consequent increase in the REM sleep latency. Moreover, it is possible that the use of these drugs could alter the dopaminergic system, downregulating the nigroestriatal system activity, leading to an increase in the PLM frequency.
haloperidol twelve patients developed a neuroleptic-induced parkinsonism (NIP), while the other ten patients did not experience any extrapyramidal-motor side effects. Patients with extrapyramidal symptoms had a significantly shorter sleep duration (392±63 min vs. 453±26 min), a higher number of nocturnal awakenings (26±16 vs. 14±9) and an increased percentage of wake compared with the symptom free patients (16±9% vs. 8±4%). Patients with extrapyramidal symptoms also exhibited a significant higher number of PLM per hour (PLM-index) during sleep (12±9 vs. 5±3). Nine of 12(75%) patients with extrapyramidal symptoms had a PLM-index > 5 and 7 (58%) also had a PLM-arousal-index >5. In the ten control subjects three had a PLM-index >5 and only one a PLM-arousal-index >5.

Conclusion: Lowering of dopamine levels by neuroleptic medications is associated with the emergence of periodic leg movements in schizophrenic patients.

Other Movement Disorders

P 107
Sleep-wake disturbances in 139 consecutive patients with Parkinson’s syndrome

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Background: Sleep-wake disturbances in patients with Parkinson’s syndrome (PS) are frequent. Most studies were focused on patients with idiopathic Parkinson’s syndrome (Parkinson’s disease) and/or on only few sleep-wake disturbances (excessive daytime sleepiness (EDS), insomnia). Aims: The aim of the study was to establish the frequency of a variety of sleep-wake disturbances in a non-selected series of patients with PS of variable etiology.

Patients and methods: Over a 1-year period 139 consecutive patients with PS were assessed. There were 48 (34%) women and 91 (65%) men with a mean age of 67±10 years (range: 36-88). Diagnoses included Parkinson’s disease (PD, 84%) and atypical Parkinsonism (16%). The frequency and type of sleep-wake disturbances were assessed by a standard questionnaire. Data on severity and duration of PS, and medications were also noted.

Results: The mean duration of PS was 8±6 years (range: 0–29). The mean UPDRS-III score was 24±12 (range: 4–78). Ninety (65%) out of 139 outpatients reported sleep-wake disturbances, and 15% were taking sleeping pills. The most common disturbances were sleep maintenance insomnia (30% out of 139 patients), EDS (28%) and a history, suggestive of REM sleep behavior disorder (20%). Sleep onset insomnia (7%), restless legs symptoms (11%), and nightmares (13%) were less commonly reported. The mean Epworth sleepiness score (ESS) was 11 (range 3–20), and in 15% of the patients the ESS was > 10. In six patients, four of whom with atypical parkinsonism, RBD was the first symptom of PD.

Conclusion: We confirm the high frequency of sleep-wake disturbances (mainly insomnia, EDS and RBD) in PD, and suggest that multiple factors may be involved in their occurrence. Keywords: Parkinson syndrome, sleep disturbances

P 108
Sleep-wake disorders in patients with Parkinson’s syndrome: Review of 31 patients referred to a sleep center

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Background: Only very few studies reported the results of neurophysiological studies in patients with Parkinson’s syndrome (PD) and sleep-wake disturbances.

Aims: To report the results of sleep-wake studies in 31 consecutive patients with PD and sleep-wake complaints referred to our sleep laboratory. Patients and methods: There were 7 (23%) women and 24 (77%) men with a mean age of 63±10 years (range: 45-88). Diagnoses included Parkinson’s disease (PD, 68%) and atypical Parkinson’s syndrome (32%). The most frequent referral complaints/disturbances were suspected REM sleep behavior disorder (RBD, 74%), excessive daytime sleepiness (EDS, 45%) and suspected sleep-disordered breathing (SDB, 23%). Polysomnography (n=31), multiple sleep latency test (MSLT, n=20) and 2-week wrist actigraphy (n=9) were recorded and scored using standard criteria.

Results: The most frequent polysomnographic findings included an increased muscle tone in REM sleep (65%), a sleep efficiency <85% (54%), and decreased/absent sleep spindles (52%). RBD (45.2%), SDB (apnea-hypopnea index >10/h, 38%) and periodic limb movements in sleep (PLMS >10/h, 26%) were found less frequently. The mean sleep latency on MSLT was <8 minutes in 12 (60%) and <5 minutes in 5 (25%) out of 20 patients. Sleep onset REM periods (SOREM) were observed in 5 (6%) of 86 naps. In seven (77%) of nine patients actigraphy documented abnormally increased mean rest/sleep periods per day (> 40%).

Conclusion: Increased muscle tone in REM sleep, sleep maintenance insomnia, reduced spindle activity, short mean sleep latencies on MSLT and increased rest/sleep amounts on actigraphy are the most common
objective sleep-wake findings in patients with PD and sleep-wake complaints. The frequency of SDB, PLMS, and SOREM is less than reported in previous works. Keywords: Parkinson syndrom, polysomnography, multiple sleep latency test

P 109
Polysomnographic Findings in Progressive Supranuclear Palsy

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Introduction: Rem-Sleep-Behaviour-Disorder (RBD), loss of slow-wave-sleep, PLMS and sleep fragmentation are the polysomnographic hallmarks of neurodegenerative diseases presenting with Parkinson syndromes. While PD and MSA as synucleinopathies show similar disturbance patterns, PSP as a tauopathy presents several characteristic features, which may eventually aid differential diagnosis. Previous findings suggest no or only preclinical RBD, sleep disruption and no respiratory abnormalities in sleep.

Objective: To establish typical polysomnographic findings in PSP.

Patients and Methods: 11 patients (3 women, 8 men, mean age 68 yrs.) with PSP according to British Brain Bank criteria were examined in our sleep laboratory. Overall sleep efficiency, sleep stage distribution, the degree of sleep fragmentation, PLM index, motor activity during Rem phases as well as subjective judgement of sleep quality assessed by PDSS were evaluated.

Results: Polysomnographic recordings showed a reduction of sleep efficiency (mean 56.8%, range 38.5–85.2%), sleep fragmentation with 7–34 awakenings, loss of slow wave sleep (mean 18%, range 0–25.7%). Rem sleep, characterized by a marked reduction of rapid eye movements, was determined with a mean of 23%, showing a widespread range from 0-58.6%. 3 patients showed RBD, 3 patients had a pathologic respiratory distress index. A pathologic PLM index with an average of 116.7/h (range 6.7–273.5) was registered in all patients, none however complained of involuntary leg movements or restless legs syndrome. Only one patient judged his sleep quality as poor (1.8 on PDSS Parkinson’s Disease Sleep Scale; range from 1-very poor to 8-excellent).

Conclusion: Loss of rapid eye movements in Rem sleep, but sometimes severe RBD as in synucleinopathies, severe destruction of normal sleep architecture and especially a gross misperception of sleep quality distinguish sleep in PSP, reflecting neurodegeneration and progressive cognitive impairment.

Neuromuscular Disorders

P 110
The Relationship of Fatigue to Daytime Sleepiness in Myotonic Dystrophy

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Aims: Both daytime sleepiness and fatigue are prominent symptoms of myotonic dystrophy (DM). The only two studies that have assessed the relationship between these symptoms suggested that they constitute independent features of DM (n=36, Rubinsztein et al., 1998, JNNP; n=32, van der Werf et al., 2003, JNNP). The aim of the present study was to verify, in a large sample of DM patients, whether these symptoms are distinct clinical entities of the disease.

Methods: Two-hundred adult DM patients (79 men, 121 women; mean age (SD) 47.0 (11.8) years) completed the Epworth Sleepiness Scale (ESS), the Daytime Sleepiness Scale (DSS) specifically devised for DM (Laberge et al., 2004, JSR), the Chalder Fatigue Scale (CFS), and the Krupp Fatigue Severity Scale (KFSS). All patients were examined by a neurologist and had their muscular impairment categorized as mild (n=41), moderate (n=36), or severe (n=123). Mean (SD) number of CTG repeats was 809.2 (529.4). Pearson product-moment correlation coefficients and Spearman non-parametric rank correlation coefficients were used.

Results: The mean (SD) scores were 8.1 (5.0) for ESS, 4.9 (3.0) for DSS, 5.1 (3.0) for CFS, and 4.6 (1.7) for KFSS. Both the DSS and KFSS were related to muscular impairment (r=.37 and r=.27, p<.001) while only the KFSS was related to CTG repeat (r=.21, p<.01). The CFS and KFSS correlated more highly with each other (r=.74, p<.001) than with either daytime sleepiness rating scales (r’s varying between .49 and .63, p<.001). Conversely, the ESS and DSS correlated more highly with each other (r=.64, p<.001) than with either fatigue rating scales.

Conclusions: The data reveal a significant overlap between fatigue and daytime sleepiness in DM. Since the pathways for treating daytime sleepiness may substantially differ from those specific to fatigue, clinicians should thoroughly inquire about sedentary activities, sleep schedules, and functional limitations of DM patients in an effort to separate “true” fatigue from “true” daytime sleepiness and to complement subjective rating scales by other methods of assessment.

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P 111
Sleep disorders in patients with myasthenia gravis

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Aim: The aim of this study was to assess the prevalence of sleep disorders among the patients with myasthenia gravis.

Methods: We have used the following scales: Soldatos Insomnia Scale (SIS), Epworth Sleepiness Scale (ESS), Sleep Disorders Questionnaire. We have also used a five-item screening questionnaire for Restless Legs Syndrome (RLS), based upon the International Restless Legs Syndrome Study Group. The scale and questionnaires were sent by mail to the patients of Myasthenia Gravis Out-Patient Department, Department of Adults’ Neurology, Medical University of Gdansk, Poland. The questionnaires were anonymous.

Results: We have sent questionnaires to 100 patients with myasthenia. We have received questionnaires from 73 subjects (18 M and 55 F). The mean age of the examined group was 48.9 years. The mean score in the SIS was 15.5 points and in the ESS 11.8 points. Thirty-eight (52%) subjects reported problems with falling asleep. Thirty-two subjects (43.8%) had symptoms of RLS. The patients suffered from following sleep disorders: periodic limb movements (39.7%), frequent awakenings (58.9%), sleep paralysis (24.6%), sleep-disordered breathing (46.4%), bruxism (20.5%), sleep behaviour disorders (12.3%), somnambulism (5.4%), nightmares (17.8%), uncontrolled daytime naps (23.2%).

Conclusion: Sleep disorders are common among patients with myasthenia gravis. Although their treatment may be difficult due to the effect of the hypnotics on the muscle tension it may lead to improvement of the quality of life of patients with myasthenia gravis.

P 112
No sign of RBD in hereditary spinocerebellar ataxia (SCA-2) patients

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Introduction: The study investigated the sleep profile of a homogeneous group of patients suffering from hereditary spinocerebellar ataxia (SCA-2). Unique to this group of patients is the early degeneration of the olivopontocerebellar region of the brainstem. In the course of disease progression, additional structures such as the thalamus, substantia nigra, and the anterior horn are also affected. By contrast, there is no sign of cortical involvement until a very advanced stage of the disease. The olivopontocerebellar region has been associated with the control of REM sleep initiation. The thalamus, in particular the nucleus reticularis thalami, is regarded as the rhythm generator of NREM sleep. Together with the midbrain, the thalamus is believed to be involved in maintaining muscle atonia. Accordingly, it was expected to find a loss of muscle atonia already at an early stage of the disease, accompanied by alterations of REM sleep with reduced to absent REM sleep episodes as a function of disease progression. With regard to SWS, no specific hypotheses were expressed.

Method: Standard PSGs (Brainlab, Schwarzer, Munich) were recorded for 9 patients on 2 consecutive nights. Records were scored visually by two experienced raters according to R & S and ASDA criteria. Patients differed only in disease severity and disease progression. Subjectively, all patients slept well. Only the mildly affected patients reported a dream recall. Polysomnographic findings were analysed with regard to disease duration, polyglutamine expansion size (CAG count), age of onset, ataxia score, age, and sex.

Results: Sleep efficiency was poor in all 9 patients, due to expansive periods of nocturnal wakefulness. Sleep onset latencies were inconspicuous. The more severely affected patients showed an increase in amount of SWS. REM sleep was strongly reduced or absent in these patients. In all severely affected patients, REM sleep was without atonia. There was no indication of RBD or RBD-like behavior in any patient. Trend analyses suggest that an increase in SWS as well as a decrease in REM sleep differentiate well between different stages of disease progression.

Discussion: In spite of subjective reports of good sleep, objectively, SCA2 patients displayed poor sleep efficiency and increased sleep fragmentation. Several sleep parameters compare to those reported for Idiopathic Parkinson’s Disease. SWS and REM sleep appear to be a promising progression markers in SCA-2.

P 113
Sleep quality in autosomal-recessive Parkinson Syndrome (Park 6)

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Introduction: Patients suffering from Idiopathic Parkinson’s Disease (IPD) often complain about poor sleep...
quality. Specifically, they report a high incidence of nightmares and reduced total sleep time. PSG findings show a prolonged sleep onset period, reduced sleep efficiency and increased sleep fragmentation. Since IPD patients are a heterogeneous group with regard to pathogenesis, it should be interesting to investigate subjective and objective sleep parameters of Parkinson patients who are homogeneous with regard to disease etiology, such as patients suffering from PARK6, a familial autosomal-recessive form of PD caused by a mutation of the PINK1-gene which codes for a serin-threonin-kinase with mitochondrial localisation. Clinically PARK6 is characterized by an early onset, slow progression, continuous L-DOPA responsivity and lack of atypical attributes. The present study reports on a Spanish family with PARK 6 Parkinson-Syndrome. Of the 7 siblings, 3 were genetically homozygote and severely affected, 3 were heterozygote and clinically asymptomatic and one sibling was unaffected. Research questions concerned possible differences in sleep recordings between homozygote and heterozygote or unaffected siblings and similarities of PARK6 and IPD sleep profiles.

Method: Siblings reported no incidence of depression, increased daytime somnolence or improvement of motoric symptoms following sleep (sleep benefit). All siblings rated their sleep quality as good. Standard PSG was recorded during 2 consecutive nights using a 32-channel polysomnograph (Brainlab, Schwarzer, Munich). Records were scored visually by two experienced raters according to R & S criteria.

Results: All patients had inconspicuous sleep onset latencies. The homozygote affected patients had increased sleep fragmentation due to elevated arousal indices. Amounts of SWS and REM sleep were significant indicators of disease progression in trend analyses, showing a strongly increased amount of SWS (37%) and reduced REM sleep (6%) in the most affected patient. One asymptomatic sibling suffered from sleep apnea, all other siblings showed no sign of respiratory abnormalities, increased limb movements or RBD-like behavior during sleep.

Discussion: Aside from higher sleep fragmentation and increased arousal frequency in homozygote patients, there was no systematic difference between homozygote and heterozygote siblings. However, it should be noted that disease progression was accompanied by a heightened amount of SWS coinciding with reduced REM sleep, suggesting these parameters to be a potential marker of disease progression. Concerning IPD vs. PARK6, the latter had a good subjective sleep quality, and a more intact sleep architecture, independent of dopaminergic medication. Concerning dream content, patients reported no incidence of nightmares. Implications of these findings are addressed.

Circadian Rhythm Disorders

P 114
Influence of Commencement of Shift Work on the Sleep-Wake Cycle and Quality of Sleep

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Introduction: Many studies described the disturbing influence of shift work, especially night shifts, on sleep-wake-cycles and sleep quality. While most examinations focused on subjects with a long-term experience of shift work, little is known about young adults working the first night shifts of their life. In this study nurse students were examined prospectively by using ankle actigraphy, sleep logs and questionnaires.

Methods: 30 nurse students, mean (SD) age 20.2 (2.1) years, underwent two periods (P1 and P2)-each of 21 days-of actigraphy (ACT), using ActiTrac monitors (IM Systems Inc.) . P1 took place during an education period in nursing school, running a regular work-schedule, P2 during the following practice period in hospital including shift changes and 3-5 consecutive night shifts. Subjects filled in daily sleep logs and Epworth Sleepiness Scale (ESS) at the beginning and the end of each period. Analysis of ACT recordings using ActiTrac software (automatic scoring algorithm) provided sleep duration, sleep efficiency and sleep activity for each sleep period. Total sleep time per day (TST/d) and sleep fragmentation (number of sleep periods per day) were derived from this data. Days of night shift (N) and the 7 days following night shift (F) were taken as separate scoring periods from P2. F was matched with a 7 day reference period (R) from P1.

Results: Mean (SD) TST/d increased from 451 (37) min during P1 to 466 (36) min during P2 (P = 0.007). In opposite, regarding only night shift days (N), TST/d was significantly shorter than in P1: 404 (66) min (P = 0.001). During the days following night shift (F), TST/d was 470 (52) min which is a significant increase both compared to N (P = 0.0001) and to the reference period (R) from P1 (448 (41) min, P = 0.045). Sleep fragmentation slightly increased from 1.18 (0.13) periods per day in P1 to 1.23 (0.16) in P2 (P = 0.046). All other results for sleep fragmentation as well as sleep efficiency and sleep activity showed no significant changes, neither between P1 and P2 as a whole nor during night shift and subsequent days. ESS score went from 7.2 (2.6) points at the beginning of P1 to 7.6 (3.5) at the end of P2 which is no significant change either.

Conclusions: Under shift change conditions, total sleep time per day as well as sleep fragmentation were higher than under a regular work-schedule. We found a reduction of TST/d under night shift conditions but a prolongation during subsequent daytime shifts. The latter might show compensation for lost sleep time. Changes in sleep duration were
not accompanied by significant changes of sleep quality as far as it can be derived from ACT and ESS. This might be a hint for better adaptation to shift work among young adults and for less disturbing influences of night shift in early working life. Further research is needed to qualify these findings and compare adaptation to shift work among different age groups and states of shift work experience.

P 115
Sleepless in Alaska and Siberia: Cross-Validation of Hierarchical Factor Structure of Individual Adaptability of the Individual Sleep-Wake Cycle

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Objectives: Some results of psychometrical evaluation of chronotypological questionnaires point on the multi-dimensional nature of the adaptive ability of individual sleep-wake cycle. However, the exact factor structure of the individual wake-sleep-ability still remains to be clarified. The study was designed to cross-validate the factor structure of this ability.

Method: The English and Russian versions of 4 chronobiological questionnaires were administered to 160 students of the Novosibirsk State University, respectively.

Results: The psychometrical analysis revealed a hierarchical structure with 3 superfactors identified as “circadian lateness” (or “morningness-eveningness”), “ sleepliability” and “wakeliability”, 5-6 main factors identified as “morning and evening lateness”, “night and anytime sleepliability” and “night and anytime wakeliability”, and, at least, 15 subfactors corresponding to the primary or specific adaptive abilities of individual sleep-wake cycle.

Conclusion: The agreement between factorial structures of the English and Russian versions indicates that the subjectively assessed features of the sleep-wake cycle reflect the underlying inter-individual differences in the mechanisms of chronophysiological regulation.

P 116
No association of a Per3 clock gene polymorphism and ADHD-related idiopathic chronic sleep onset insomnia

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Background: Idiopathic chronic sleep onset insomnia (SOI) in children with Attention Deficit/Hyperactivity Disorder (ADHD) resembles much to the delayed sleep phase syndrome, and, therefore, could be considered a circadian rhythm sleep disorder. A 4/5-repeat length polymorphism of the clock gene Per3 has been found related to the delayed sleep phase syndrome and, therefore, may associate with ADHD-related chronic SOI as well. We investigated the association between ADHD-related idiopathic chronic SOI and the Per3 length polymorphism.

Methods: In 10 psychotropic-medication naive children with rigorously diagnosed ADHD and SOI (ADHD-SOI) and in 10 normal controls. the 4-and 5-repeat alleles of Per3 were analysed by PCR in DNA extracted from cheek swab samples. Actigraphic sleep onset and sleep duration and salivary dim light melatonin onset (DLMO) were evaluated in ADHD-SOI.

Results: The 4-repeat allele frequency was lower in ADHD-SOI (=0.65) than in normal controls (=0.75) (p = 0.73) with odds ratio of 0.62 (CI 0.16-2.4). In ADHD-SOI, mean (+ SD) DLMO (21:38±0:50 h), sleep onset (22:17±0:46 h), and sleep duration (9:26±0:41 h) were not significantly related to the 4-repeat allele frequency.

Conclusions: These findings suggest no association between ADHD-related idiopathic chronic sleep onset insomnia and a Per3 clock gene polymorphism.

P 117
Prevalence of delayed sleep phase syndrome (DSPS) and advanced sleep phase syndrome (ASPS) in a young adult sample

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Introduction: There is a relative dearth of studies conducted with adequate methodology about the prevalence of Circadian Rhythm Sleep Disorders (CRSD). One study (Schrader et al, 1993) found a prevalence of DSPS of 0.17% without correlation with age, and no cases of ASPS were found. The aim of this study was to assess the prevalence of DSPS and ASPS in a young adult population.

Methods: A total of 1714 questionnaires were given in an in-class survey. Of those 1276 (74.45%) were validly completed. The percent of men was 26.2; the mean age was 18.74 (±1.24) years with a range of 16-23. Questionnaire: The questionnaire includes: (1) socio-demographic information, (2) Sleep environment, (3) Sleep habits, (4) Horne & Ostberg Questionnaire (MEQ), (5) Sleep disorders, (6) Epworth Sleepiness Scale (ESS), (7) Life style, including physical activity, use of psychoactive drugs and eating
habits, (8) Health status, (9) Academic performance, (10) Recent events and behavior. A decision tree (see Results section) was used to define DSPS and ASPS.

Results: A final prevalence of DSPS of 0.7% was found after screening the whole sample according to the following consecutive steps: A) a. To have difficulty falling asleep (DFA) at night and falling asleep later than desired, and b. To have difficulty waking up in the morning. B) Not to have difficulty staying asleep (DSA) and/or early final awakening. C) No to have an irregular sleep-wakefulness pattern, D) Being evening type in the MEQ, E) Sleep onset after 2 a.m. throughout the whole week. No cases of ASPS were found according to the following steps: (A) a. To feel very sleepy in the evening falling asleep before than desired time, and b. To wake up before the desired time in the morning, (B) Not to have DFA and/or DSA, (C) The same as in C for DSPS, (D) Being morning type in the MEQ, (E) To wake up before 5 a.m.

Conclusions: Our results on prevalence of DSPS and ASPS are similar to those of previous studies (Schrader et al., 1993) but showing a higher proportion on DSPS. The age of our sample could be a partial explanation for this.

P 118
Sleepless in Alaska and Siberia: Cross-validation of factor structure of the individual adaptability of the sleep-wake cycle
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Background: Some results of psychometrical evaluation of chronotypological questionnaires point on the multi-dimensional nature of the adaptive ability of individual sleep-wake cycle. However, the exact factor structure of this ability and the physiological factors underlying the variety of subjectively assessed individual traits of the sleep-wake cycle still remain to be clarified. The study was designed to cross-validate the factor structure of the sleep-wake adaptability and to suggest a model explaining its multi-dimensional nature.

Method: The English and Russian versions of 4 chronobiological questionnaires (Horne, Åstberg, 1976; Folkard et al., 1979; Putilov, 1987, 1990, 1997) were administered to 160 students of the University of Alaska Anchorage and to 180 students of the Novosibirsk State University, respectively.

Results: The factorial structures of the English and Russian versions of the questionnaire were found to be almost identical. The psychometrical analysis revealed a hierarchical structure with 3 superfactors on the top of this hierarchy. The suggested physiological model predicts that the hierarchical multi-dimensional structure of the sleep-wake adaptability might be produced by combination of just three underlying physiological factors.

Conclusion: The results suggest that the subjectively assessed features of the sleep-wake cycle reflect the underlying inter-individual differences in the mechanisms of chronophysiological regulation.

Parasomnia

P 119
Parasomnias Could Have Adaptive Functions
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Aims: Parasomnias (P.) are brief disturbances in the body during sleep. P. are explained presently as incomplete arousals from NREM or dissociated phenomena of REM sleep. Could P. have an adaptive function, i.e. to stabilize or switch sleep stages? Primary Nocturnal Enuresis (PNE), as the most common parasomnia, was chosen as a clinical model to investigate this question.

Method: The history and clinical course of 365 patients with PNE, 9-18 years of age, were reviewed using a factorial analysis to select the most common factors. 33 PSG’s (sleep studies) of 21 enuretic children were compared with 20 PSG’s of non-enuretic children matched by age and sex. 12 PSG’s were repeated at least 6 months after treatment or “self-cure”. Standard methods of PSG scoring were performed by certified polysomnographers.

Results: Five statistically significant factors were presented as a PNE “syndrome”: 1. Bedwetting in sleep; 2. Fluctuations of daytime alertness; 3. Changes in sleep architecture; 4. Resistance to treatment (suppression of the symptom); 5. Spontaneous disappearance of bedwetting (self-cure) or deterioration (increased frequency and/or appearance of other P). The distribution of sleep stages in PNE were different from the control: Type 1: The first cycle was longer with a predominance of stage 4. Type 2: Predominance of stage 2 with frequent awakenings, and Type 3: Disorganized sleep structure. Probabilities of bedwetting (B.) were dependent on the length of each stage: stage 2–26.7%, stage 3–31.2%, stage 4–35.7%, REM-6.4%. After a B. event, the sleep stages were switched to another stage in 64.7% of the cases (mostly to REM or awake) within a few minutes, thus B. was found to occur predominantly between stages. Cluster appearances of B. episodes followed dynamic chaos patterns. B. had several
forerunning” PSG characteristics and was therefore predictable: delta wave paroxysms, high spontaneous SGR, change in heart rate variability and amount of movements. After the B. event, the sleep structure and EEG “normalized”. Repeated PSG’s after 6 months of dry period due to “self-cure” or treatment were found to be identical to the control.

Conclusion: PNE Syndrome reflects involvement of the sleep-wake mechanisms in its genesis. “Normalization” of sleep structure after an enuric episode and resistance to suppression and “self-cure” suggest that bedwetting could have an initially protective (compensatory- or adaptive) function as a physiological “switch” or “stabilizer” of immature sleep mechanisms. The adaptive patterns of bedwetting fit principles of a control system theory. Treatment of PNE should be not in the suppression of the main symptom, but in the correction of underlying problems in sleep mechanisms. Further research is needed to evaluate whether other P. might also have an adaptive function.

P 120
Confusional arousals, somnambulism or epileptic seizures?

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Purpose: Our objective is to evaluate the use of video-EEG-monitoring in differentiating parasomnias from nocturnal epilepsy.

Methods: We present a 48-year old patient with a history of nocturnal paroxysmal disorder characterised by confusion, sleep-walking and amnesia, observed several times a month for more than ten years. Epileptic phenomena were never identified since he came to us at night, after he was found unconscious with clinical signs of a tonic-clonic seizure. EEG recordings at daytime, MRI and further diagnostic procedures were not contributory in the diagnosis of nocturnal episodes. Therefore we started a continuous video-EEG-monitoring.

Results: Three ictal events with bilateral paroxysmal rhythmic EEG pattern and interictal discharges in the right temporal region were recorded after midnight. Because of subtle clinical symptomatology (eye opening, bulbus deviation to the left, oral automatism), the seizures were hardly recognizable by video-monitoring, in contrast to postictal arousals.

Conclusion: Partial seizures are an important differential diagnosis to parasomnias (particular somnambulism). The epileptic activity is often undiagnosed in polysomnograms. EEG ictal registration with twenty-channel-EEG and video-monitoring are suitable diagnostic modalities to find the proper diagnosis.

P 121
Nocturnal Groaning: Two Case Reports

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Introduction: Nocturnal groaning has only recently been reported as a new distinct type of parasomnia. It presents with episodes of expiratory groaning in sleep, predominantly during the NREM 2 and REM sleep stages, without impairing the sleep architecture or causing daytime symptoms.

Patients and Methods: Two patients (1 male, 1 female) aged 17 and 24 years with nocturnal groaning underwent neurological examination, routine biochemical tests, electroencephalography (EEG), neuroimaging, nocturnal polysomnography (PSG) and psychological examination. The patient with reported daytime sleepiness underwent multiple sleep latency test (MSLT).

Results: In patient 1 all investigation except for nocturnal PSG were normal. Nocturnal PSG showed frequent episodes of nocturnal groaning during NREM 2 and REM sleep without arousals. The sleep architecture was normal. In patient 2 neurological examination was abnormal (residual symptomatology after head trauma: mild left-sided hemiparesis, oculomotor palsy and mild organic psychosyndrome). EEG showed a slow-down of the background activity. MRI of the brain was normal. Psychological tests proved slight cognitive impairment. Nocturnal PSG revealed sleep fragmentation caused by repeated arousals from REM and NREM 2 sleep associated with stereotypical expiratory groaning sounds. The increase of wakefulness and NREM 1 sleep and the reduction of REM sleep was marked. The patient complained of excessive fatigue and daytime sleepiness, restless sleep, episodes of nocturnal eating behavior. MSLT proved slightly shortened mean sleep onset latency.

Conclusion: Based on the case report 2 we can presume that nocturnal groaning is not only a benign condition as described in the literature but also a source of interference with the quality of sleep. As only a few cases (of nocturnal groaning) have been reported to date, this type of parasomnia requires further studies to be better understood.

P 122
Multiple confusional arousals mimicking nocturnal seizures in a single night

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Introduction: Confusional arousal (CA) is a partial arousal disorder, which generally occurs during slow wave sleep as a single episode. Multiple episodes of CA in a
single night have not been reported and may be mistaken for nocturnal seizures.

**Objective:** To report the occurrence of multiple episodes of confusional arousals in a single night in children.

**Methods:** Six patients (Pt 1 An 11 yr old boy; Pt 2: a 13 yr old brother of pt 1; Pt 3: A six year old boy; Pt 4: A 4 year old girl; Pt 5: A 5 yr old boy; Pt 6: A 9 yr old boy) presented with history of multiple episodes of nocturnal spells. During the spells the subjects would sit up in bed, look confused and unresponsive without fearful appearance and after several minutes would go back to sleep. On some occasions when the mother forced patient 1 to lie down, he started struggling and sleep walking. None of them had clonic movement, tongue biting or urinary incontinence. These spells occurred both in the early and late part of the night.

**Results:** Video polysomnography study including 16 channel EEG recording showed 2–4 episodes of arousals with behavioral confusion but without choreoathetoid, ballismic or clonic movements, epileptiform discharges or sleep apnea. Patient 3 was treated by several neurologists with anticonvulsant without benefit for a mistaken diagnosis of nocturnal seizure and in patient 4 a diagnosis of partial complex seizure was strongly considered. Pt 5 also had ADHD and moderate sleep apnea with an AHI of 21/hr.

**Conclusion:** Confusional arousals are a very common occurrence in children. It has mostly been described as a single event in one night in the literature. We present six cases with same event occurring multiple times in a single night. It is important to be aware of these unusual manifestations of CA from which the youngster will generally outgrow. These can also be mistaken for seizures. The clues are the occurrence of EEG arousals usually from slow wave sleep without epileptiform discharges and the behavioral confusion without abnormal movements or response to anticonvulsants. A correct diagnosis will eliminate unnecessary costs and adverse effects of anticonvulsants.

**Hypersomnolence**

**P 123**

**Nocturnal baroreflex sensitivity in OSAS: a marker of excessive daytime sleepiness**

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**Aims:** Obstructive sleep apnea syndrome (OSAS) is the most common cause of excessive daytime sleepiness (EDS) among patients evaluated at sleep disorders centers, but it is usually very difficult to find a clear association between the OSAS severity and degree of EDS. We tested the hypothesis that baroreflex sensitivity during sleep in OSAS constitutes a neurophysiological marker of diurnal hypovigilance.

**Materials and Methods:** We studied 53 OSAS patients, 46 men and 7 women; mean age 48 ± 10.9 years, mean body mass index (BMI) 29 ± 6.2 kg/m². All patients underwent a nocturnal polysomnography. Arterial blood pressure was monitored continuously and non-invasively during the night and a Multiple Sleep Latency Test (MSLT) was done on the next day. We analyzed the correlation between EDS (MSLT value) and apnea-hypopnea index, arousal index, IDEA (Integrated Desaturation Apnea Index), minimum SaO², baroreflex sensitivity (BRS) (Sequence Technique), heart rate variability (HRV), difference (delta) of the systolic blood pressure, diastolic blood pressure, and heart rate (RR interval) following apneas. A RRI spectrogram was obtained from each recording by computing power spectra over a running data-window of 110 s duration. Spectral powers were calculated in the low frequency (LF) band, from 0.05 to 0.15 Hz, and in the high-frequency (HF) band, from 0.15 to 0.50 Hz, deriving the LF/HFpower ratio, an indirect measure of heart sympatho-vagal balance. To model the relationship between MSLT and all polysomnographic independent variables and particularly to determine the most influential factor in daytime sleepiness a Multiple linear regression analysis (backward step-wise regression) was performed.

**Results:** According to their MSLT values, 14 patients were classified as nonEDS and 39 as EDS. Overnight values of blood pressure were similar in EDS and nonEDS patients and the mean RR interval did not differ significantly between EDS and nonEDS. BRS was significantly lower and the LF/HF ratio was higher in EDS patients. MSLT and BRS showed significant positive correlation (the greater the somnolence, the lower the BRS) during the awake and REM sleep phase. BRS was significantly higher in nonEDS compared to the EDS group during stages Wake, 1-NREM and REM sleep. MSLT and LF/HF ratio showed a negative correlation (the higher the LF/HF ratio, the greater the somnolence) in Wake and NREM sleep.

**Conclusions:** Our results suggest that EDS in OSAS is better explained by baroreflex sensitivity and the LF/HF ratio, probably measuring the same physiological mechanisms. OSAS patients without EDS show a sleep phase-related modulation of BRS significantly different from patients with EDS.

**P 124**

**Excessive Daytime Sleepiness in Patients with Internal Diseases**

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**Introduction:** Symptoms like fatigue, tiredness, apathy are widely presented in a hospital population and thus could lead to the misdiagnosis of excessive daytime sleepiness (EDS). The purpose of our study was to estimate the prevalence of complaints on EDS among the hospital patients and to compare it to the objective data.

Subjects and Methods: 350 patients consequently admitted to the hospital during 1 month with the diagnosis of internal diseases (non-neurological, psychiatric, surgical or gynecological) were included into the study (214 females, 136 males, mean age 62.0±15.0 yrs) . 150 patients rejected to participate (mean age 64.5±14.4 vs 60.3±15.2 yrs, 59% vs. 63% females comparing with the compliant group). Epworth sleepiness scale (ESS), subjective sleep quality scale (SSQS), sleep apnea screening questionnaire (SASQ), hospital anxiety and depression scale (HADS) were used. MSLT was performed for 7 randomly selected patients with ESS score >7.

Results: EDS was found in 96 (48%) of studied patients. Only 48 (50%) of them had subjective complaints on disordered sleep according SSQS and 52 (54%) could have obstructive sleep apnea syndrome according SASQ. Many patients with high ESS score had pathological anxiety 38 (39.6%) and depression 23 (24.0%) score (>7) according HADS. They had significantly (p<0.05) higher mean anxiety score (7.1±4.0 vs. 5.3±3.6) than the patients with low ESS. Sleep latency by MSLT was found abnormal (<5 min) only in 1 patient from 7. Mean ESS score significantly correlates (r=0.2) with the HADS anxiety score and SASQ score (r=0.18).

Conclusion: We revealed high prevalence of EDS in the population of hospitalized patients with somatic diseases. About half of the EDS cases could be associated with the disordered sleep or sleep apnea. MSLT rarely confirms pathological sleepiness in these patients.

**Epilepsy in Sleep**

**P 125**

Sleep-wake habits and disorders in a series of 100 adult epilepsy patients-a prospective study

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Aims: To assess sleep-wake habits and disorders (including excessive daytime sleepiness (EDS)) in an unselected outpatient epilepsy population.

Methods: Sleep-wake habits and presence of sleep disorders were assessed by means of a clinical interview and a standard questionnaire in 100 consecutive epilepsy patients and 90 controls. The questionnaire and includes three validated instruments: the Epworth Sleepiness Scale (ESS) for excessive daytime sleepiness (EDS), SA-SDQ for sleep apnea (SA), and the Ullanlinna Narcolepsy Scale (UNS) for narcolepsy. Epilepsy related variables including type of epilepsy, frequency of seizures, and number of antiepileptic drugs were also assessed.

Results: The estimated average total sleep time was similar in both groups. Insufficient sleep times were suspected in 24% of epileptics and 33% of controls. Sleep maintenance insomnia was more frequent in epileptic patients (52% vs 38%, p=0.06), whereas nightmares (6% vs 15%, p=0.04) and bruxism (10% vs 19%, p=0.07) were more frequent in controls. Sleep onset insomnia (34% vs 28%), EDS (ESS<10, 19% vs 14%), SA (9% vs 3%), RLS (18% vs 12%) and most parasomnias were similarly frequent in both groups. In a stepwise logistic regression models loud snoring and RLS were found to be the only independent predictors of EDS in epileptics.

Conclusions: Sleep-wake habits and the frequency of most sleep disorders (with the exception of sleep maintenance insomnia, nightmares, and bruxism) are similar in a non-selected epilepsy patients as compared to controls. In epilepsy patients, EDS was predicted by a history of loud snoring and RLS but not by SA or epilepsy-related variables

**P 126**

The value of EEG monitoring during night sleep in the diagnosis of epilepsy in children

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Aims: Night sleep EEG monitoring (NSEM) can be used for the diagnosis and monitoring of epilepsy treatment in children. The aim of the study was to evaluate the usefulness of NSEM in the detection of paroxysmal EEG activity in children subjected to observation due to seizure disorders.

Methods: The analysis was made on a group of 41 children admitted to the Chair and Department of Developmental Neurology, Poznan University of Medical Science in from January 2004 to February 2005 to diagnose and monitor the treatment of epilepsy, who were subjected to NSEM. The mean age of children was 10.4±5.4 years. Twenty four (58.5%) of the subjects were male and 17 (41.5%) were female. NSEM recordings were made with use of “Ceegraph Traveler” (Biologic, USA). The mean time of NSEM recording was 16.5±2.7 hours.

Results: Twenty four children (58.5%) from the group of 41 were admitted to diagnostic evaluation, 17 (41.5%) for monitor the treatment. Fifteen children (36.6%) were taking
at least one antiepileptic drug (AED) on admission. The AEDs were administered in monotherapy in 10 patients (24,4%) and in polytherapy in 5 (12,2%). EEG activity during wakefulness and night sleep was recorded in all patients. Clinical events in the form of seizures were recorded in 15 (36,6%) patients, in 10 (66,7%) cases during sleep and in 5 (33,3%) during wakefulness. Correlation of the clinical event with the EEG paroxysmal activity was declared in 8 (53,3%) children. In seven patients (46,7%) the clinical event was non epileptic (arousal, sleep terror, sleepwalking, sleep starts, and other motor activity). Seizure-like event were non epileptic (arousal, sleep terror, sleepwalking, sleep starts, and other motor activity). Seizure-like epileptiform EEG changes during wakefulness were found in 17 (41,5%) patients and during sleep in 38 (92,7%). Generalised EEG changes during wakefulness were found in 20 (48,8%) patients and during sleep in 38 (92,7%).

Conclusions: The results show that the NSEM monitoring is an effective epilepsy diagnosing tool as it detects the paroxysmal activity better than the standard EEG. It also makes possible to record the EEG activity during a clinical seizure and to verify whether the seizure is of epileptic or other nature. By enabling to record EEG activity during physiological night sleep it contributes to better detection of the paroxysmal EEG activity.

P 127

Vagal reactivity during quiet sleep in neonates, as assessed by the oculocardiac reflex

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Aims: An appropriate response to a respiratory or cardiac challenge during sleep may sometimes involve arousal or a state-switching process. Although neonates show fewer episodes of bradycardia and apnoea in quiet sleep (QS) than in active sleep (AS), QS may nevertheless correspond be a vulnerable state, since arousability is lower than in AS.

Methods: To investigate this question during cardiac failure, we analyzed autonomic and behavioral responses to phasic, vagally-mediated stimulation (a 10-second oculocardiac reflex, OCR) in 50 healthy neonates (postconceptional age: 39.1 ± 1.1 weeks) during QS.

Results: Neither awakening nor behavioral escape reactions were observed but 14 out of the 50 neonates switched into non-quiet sleep. Bradycardia was systematically observed after ocular compression (duration: 12 ± 5 sec, maximal asystolia: 1047 ± 520 msec) and central apnoea (5 ± 2 sec) occurred in 86% of the neonates. During QS, the neonate’s apnoea incidence and arousability were found to be time dependent. When the OCR test occurred early in the QS episode (delay <15 min), the switch towards non-quiet sleep never occurred, and apnoea was very frequent (94%). In contrast, when ocular compression occurred late in the QS episode, a transition towards non-quiet sleep was systematically observed, along with significantly fewer apnoea events (64%, p <0.001). Biometric parameters, blood oxygen saturation and cardiac responses did not differ between the 2 groups of neonates.

Conclusion: These results demonstrate that during a QS episode, there is a progressive decrease over time in the respiratory system’s responsiveness to phasic, parasympathetic stimulation, whereas arousability increases. This finding suggests that the neonates could be more vulnerable to a fatal event when a cardiac challenge occurs in the first part of a QS episode.

P 128

Where is baby mouse sleeping? What is baby mouse sleeping with? The sleep culture in Italy from 0 to 6…18 years

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12 years ago a team for studying sleeping habits and sleep disorders during infancy, childhood and adolescence was born in Genoa (Italy), in order to formulate some guidelines for really support the infant-child-adolescent affected by sleep disorders (and outskirts). The team includes as operators members of community pediatrics-university-basic pediatrics-hospital. We wanted to compare the respective competences, in order to consolidate a network, institutionally effective and qualified, able to communicate. We decided to proceed in phases, starting from a first time (Phase 1) of training-selftraining, as we are a team of technicians working in different branches of study, having an interest in this project. The topics were: reciprocal competences; behavioural models; formulation of assistance protocols and connection protocols. In a second time (Phase 2) we tried to locate some spaces of communication-checking in order to continue (for example:parallel researches) and some spaces of communication-teaching, essential to train new technicians, able to work actively at this multidisciplinary approach. After a 0-18 yrs transversal research (1998), we are carrying out a longitudinal study at national level, that started from birth’s units, concerning the fetus-newborn and the sleep at home and in the institutions at preschool age. We take great care over gathering data as to cultural biorhythms, taking into account the recent tranformation of Italian society in multiethnic community.
P 129
Effect of medium chain triglycerides on sleep and thermoregulation of neonates during prolonged cool exposure
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Aims: Medium chain triglycerides (MCT) are an easily and rapidly-assimilated source of energy, especially for infants whose digestive functions are immature. Thus, MCTs are often supplied in milks for preterm neonates. The aim of this study was to evaluate the influence of MCT content on thermoregulation and sleep of neonates exposed to prolonged cool exposure, as can potentially be encountered in incubators where thermoneutrality is not fully achieved.

Methods: 13 neonates (gestational age: 34±3 weeks of amenorrhea; postnatal age: 24±10 days; study weight: 2.2±0.3 kg) were studied in a closed, experimental incubator. They were divided into 2 groups according to the (isonitrogenous, isocaloric) nutritional supply: an MCT group (MCT: 37% of total lipids) and a LCT group (long chain triglycerides: 100% of total lipids). The neonates were exposed to a 75-h period of cool exposure (2°C below thermoneutrality). Sleep, internal and skin temperatures and oxygen consumption (VO2) were recorded during morning naps, between 2 bottle feeds at thermoneutrality (TN=33.6±1.2°C) and during the first and last 3-h periods of the prolonged cool exposure.

Results: An inter-group difference in body temperature appeared as the cool exposure progressed. At the end of this period, the mean skin temperature was higher (+0.46°C; p=0.03) and the internal/skin temperature gradient (reflecting thermal stress) tended to be lower (-0.38°C; p=0.07) in the MCT than in the LCT group. In the MCT group, VO2 was always higher than in the LCT group whatever the thermal conditions (+31%; p<0.001). However, during the exposure, VO2 did not increase, in contrast to what was seen in the LCT group (+25%; p<0.01). During the cool exposure, the sleep duration increased in the MCT group (+18 min; p=0.04) whereas wakefulness after sleep onset tended to increase in the LCT group, (+12 min; p=0.07). As a result, the sleep duration was significantly greater in the MCT than in the LCT group at the end of the cool exposure (+37 min; p=0.02).

Conclusions: An MCT supply improved the resistance of premature neonates to prolonged cool exposure. This diet appears to preserve sleep structure, which is of major importance for an infant’s neurobehavioural development and growth.

P 130
Prolonged cool exposure and sleep in neonates
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Aims: In neonates, increased production of metabolic heat (assessed from oxygen consumption, VO2) is a typical response to a cool exposure. Oxygen consumption is higher in active sleep (AS) than in quiet sleep (QS). This difference increases when neonates are exposed to a brief, cool exposure. The aim of this study was to analyse the time-course of changes in VO2 in each sleep state during a prolonged cool exposure, such as can be encountered in incubators (since thermoneutrality is difficult to assess in routine clinical care).

Methods: 7 neonates (gestational age at birth: 34±3 weeks of amenorrhea; postnatal age: 21±13 days) were studied in a closed, experimental incubator by successive exposure to thermoneutrality (TN=33.5±1.1°C) and a 75-hour cool acclimation period (TN=-2°C). Sleep, skin and internal temperatures and oxygen consumption were measured at thermoneutrality and during the first and last 3 hours of the prolonged cool exposure.

Results: During the first 3 hours in the cool environment, an increase in AS (+13%; p=0.03) was observed at the expense of QS (a decrease of 11%; p=0.04). This change persisted right through to the end of the cool exposure. An increase in VO2 was observed at the end of the cool exposure (but not at the beginning) and was significantly higher during QS (+33%: 5.88±0.80 mL min kg⁻¹) than during AS (+20%: 5.75±0.52 mL min kg⁻¹; p=0.04).

Conclusions: In neonates, during a prolonged cool exposure, the maintenance of body homeothermy in neonates is related not only to a change in sleep structure (an increase in AS and a decrease in QS) that persists throughout the exposure but also to a sleep-state-dependent increase in heat-generating metabolic rate.

P 131
Nocturnal arterial oxygen saturation and spontaneous arousals in future SIDS victims
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Aims: Compared to control infants, victims of Sudden Infant Death Syndrome (SIDS) have a decreased arousability during sleep with fewer cortical arousals and more
frequent subcortical activations suggesting an incomplete arousal process. Activation of brainstem arousal reflexes could be a recovery mechanism from hypercapnic or hypoxic episodes. As future SIDS victims were reported to have abnormal regulation of upper airways during sleep, the present study was undertaken to evaluate the arterial oxygen saturation values before spontaneous arousals in future SIDS victims.

Methods: Twelve infants were monitored in sleep laboratories some days or weeks before they died of SIDS. Their polygraphic sleep recordings were compared with those of matched control infants. Control and SIDS infants were matched for gender, gestational age, weight at birth, age at recording and sleep position. The polysomnographic recordings were analyzed visually. Arousals were differentiated into subcortical activation or cortical arousals, according to the presence of autonomic and/or EEG changes. Oxygen saturation was recorded continuously by a transcutaneous sensor (Nellcor, USA). Median values of blood oxygen saturation were calculated for 10 sec. periods before each spontaneous arousal in REM and NREM sleep.

Results: Cortical arousals were significantly less frequent in the future SIDS victims than in the control infants during both REM and NREM sleep (p = .039). The frequency (p = .017) and duration (p = .005) of subcortical activation were significantly greater in the SIDS than in the control infants during REM sleep. No differences were found in the frequencies of subcortical arousals in NREM sleep. Oxygen saturation values were lower before cortical arousals in REM sleep (p < .001). No differences were found in NREM sleep. Oxygen blood saturation preceding subcortical activations was lower in the SIDS victims than in control infants in REM sleep (p = .027). In NREM sleep, the oxygen saturation values before subcortical activations were higher in the SIDS victims compared to control infants (p = .001).

Conclusions: Oxygen saturation values preceding subcortical activations and cortical arousals were lower in the SIDS than in the control infants during REM sleep. If these findings can be implicated in the greater frequency of subcortical activations in SIDS victims remain to be determined.

Aims: The assessment of the neonatal brain maturation during the period ranging from 33 to 45 weeks of postmenstrual age by means of sleep multichannel EEG recordings. On this purpose, two interdependence indexes among different brain areas were calculated: one sensitive to linear interdependences (CF) and a second one (N) through which nonlinear interdependences can be also detected.

Methods: Digitised monopolar EEGs of four groups of 8 healthy neonates were used for this study: (1): 33–35; (2): 36–38; (3): 39–41 and (4): 42–45 weeks. The recording electrodes were Fp1, Fp2, C3, C4, T3, T4, O1 and O2 (average as reference). During active (AS) and quiet sleep (QS), the value of the average squared coherence function CF(X ALL Y) among each electrode (X) and all the other ones (ALL Y) was calculated for the EEG low frequency band (0.5–8 Hz.). Additionally, a recent interdependence index N(X ALL Y) was calculated from the reconstructed state space of the EEG signals. The significance as well as the possible nonlinearity of the interdependence index N were assessed by using a variant of the multivariate surrogate data test. A MANOVA test was used for comparing the average values of each index among the different groups, electrodes and sleep states.

Results: CF(X ALL Y) increases significantly with age during QS for central and temporal electrodes (P < 0.01). On the contrary, index N decreases significantly with age for Fp2 and C4 during QS and for T4 and T3 during QS and AS (P < 0.01), being the values of N greater during QS than during AS (P < 0.01). The index N was found to be of nonlinear character.

Conclusions: Nonlinear interdependences among different brain areas decrease during the neonatal maturation whereas a parallel increase is observed in the linear correlations mainly during quiet sleep.

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P 133
Maturation of Spontaneous Arousals in Healthy Infants
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Aims: The propensity to arouse from sleep is an integrative part of the sleep structure and can have direct implications in various clinical conditions. This study was conducted to evaluate the maturation of spontaneous arousals during the first months of life in healthy infants.

Methods: Nineteen infants were studied with night-time polysomnography on 3 occasions: 2–3 months, 5–6 months
and 8–9 months. The infants were born full-term, were healthy at the time of study, had no history of apnea. Sleep state and cardiorespiratory parameters were scored according to recommended criteria. Arousals were differentiated into subcortical activations or cortical arousals, according to the presence of autonomic and/or EEG changes. Frequencies of subcortical activations and cortical arousals were studied at different ages in both REM and NREM sleep.

Results: During total sleep time, the frequency of total arousals, cortical arousals and subcortical activations decreased with age. The maturation of the arousal events differed according to sleep states and types of arousals. Subcortical activations decreased continuously from 2–3 months to 8–9 months of age in both REM and NREM sleep. In REM sleep, the frequency of cortical arousals increased between 2–3 months to 8–9 months of age, especially from 2–3 months to 5–6 months. In opposite, the frequency of cortical arousals in NREM sleep decreased in particular between 5–6 months to 8–9 months.

Conclusions: During the first months of life, the frequency of cortical arousals and subcortical activations decreased in healthy infants. However, the maturation process was different between cortical arousals and subcortical activations. This finding suggests a difference in the maturational sequence of the different brain centers regulating arousals.

P 134
Snoring and Behavioral Problems in Prepubertal Children

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Aims: Sleep-disordered breathing can lead to behavioral disturbances and learning deficits in children. However, scant data are available in developing countries on such an issue. The aim of this study was to compare habitual snoring with behavioral problems and academic performance in school-age children.

Methods: In Vinhedo City public schools, parents of children from 1st to 4th grade responded to pediatric sleep questionnaire. A behavioral questionnaire was applied to both parents and teachers. Only positive responses of both parents and teachers were considered. Habitual snoring (more than 4 nights/week) was compared with the behavioral and academic problems using qui-square test (p < 0.05).

Results: A total of 1107 children returned the sleep questionnaire, of which only 879 children also submitted the behavioral questionnaire. The age ranged from 7 to 12 years, with a mean of 9.9 +1.5 years. Habitual snoring was found in 16%. Habitual snoring was associated with hyperactivity, attention deficit, opositional behavior, anxiety, and academic problems. Habitual snoring was not associated with irritability or mood problems.

Conclusion: These preliminary data showed that behavioral problems and poor academic performance were frequent in school-age children with habitual snoring.

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P 135
Relationships between headache and sleep in a non clinical population of children and adolescent

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Aims: The aim of the present study was to evaluate the relationships between headache and sleep quality in a large non clinical population, through the use of self-administered questionnaires on sleep and headache.

Methods: All subjects were recruited from 4 schools of Rome and two comprehensive sleep and headache questionnaires were administered. Data were collected using a slightly modified version of School Sleep Habits Survey (Wolfson & Carskadon, 1998) that included items about sleep habits during the previous 2 weeks and three scales: (1) Sleepiness Scale; (2) Sleep-Wake Problems Behaviour Scale; (3) Morningness/eveningness scale. Further a self-report headache questionnaire about the characteristics of migraine attacks. The questionnaires were presented to 1115 subjects and 1073 children and adolescent (50.89% Males and 49.11% Females; Mean Age = 10.56; D.S. =0.50; Range = 8-15 years) completed the questionnaires (Return rate: 96.3%). Males and females did not differ for age [F(1,1071) =0.01; n.s.]. The children filled out the questionnaires individually in the classrooms, after brief group instruction on answer formats in about 30-45 minutes.

Results: Among the whole sample, 21.4% reported headache occurring at least once a week (5% everyday, 7.4% more than once a week, 9% once a week), 16.1% reported headache occurring 1-2 times in a month, and the remaining 61.5% less then once a month. Only 31 subjects (2.93%) reported that they did not suffered of any headache attack. The 49.3% of headache sufferers reported that attacks last less than half-hour, 18.0% about an hour, 4.6% about 2 hour, 18% more than 2 hours. The occurrence of the attacks was more frequent during the morning (25.6%) and the evening (26.4%), and to a lesser extent in the afternoon (11.1%); night attacks occurred in 8.3% of the subjects. It is noteworthy that 31.2% of subjects report as causative factor of their headache “a bad sleep”, while 21.9% emotional distress (hanger, sadness and worry). Using the combination duration and frequency criteria (“at least an headache attack per week” and “duration of attack equal or longer then 1 hour”) we identified 124 (11.56%) recurrent headache
sufferers. About 2/3 of Headache sufferers are Evening (E)-types while about half of headache free group are Morning (M) types. When we consider sleep habits (bedtime, risetime and total duration of sleep) and sleepiness scale total score no difference emerged between recurrent headache sufferers and the other subjects. On the other hand, significantly \( [F(1,1069) = 8.31; \ p < .01] \) higher scores in the Sleep-Wake Problems Behaviour Scale were observed between subjects with recurrent headache (Recurrent Headache Group Mean score = 34.6, S.D. = 7.6; No recurrent headache Group Mean score = 32.6, S.D. = 8.1).

**Conclusions:** Even in a non-clinical population, headache children have a stronger circadian typology preference (evening type) and have significantly higher sleep-wake problems.

**P 136**

**Comparaison of sleep characteristics and autonomic nervous system activity of children with OSAS less than three years of age who have undergone adenoidectomy and tonsillectomy**

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**Objective:** Although surgical treatment of OSAS is common practice, the surgical option is rarely taken for infants who are less than 3 years of age. Moreover, while there is strong evidence that candidates for adenoidectomy and tonsillectomy (AD/TC) suffer also from OSAS, relatively few of the surgery candidates undergo a polysomnographic examination. The indication for AD/TC surgery relies mostly on case history taken by the ENT specialist, and physical examination while the patient is awake. This study was conducted to evaluate the effect of OSA on both sleep characteristics and the autonomic nervous system of children less than 3 years of age, and their evolution post surgical treatment.

**Design:** Thirteen children, with a median age of 64 weeks (range: 43–137 weeks) (or 1.2 years, range: 0.8–2.6 years) were enrolled in the study. They underwent polygraphic recordings for a night before surgery, and again after a delay of 12 weeks (range: 4.1–23.3 weeks) post AD/TC surgery.

**Results:** All thirteen children suffered from OSAS, with a median obstructive apnea index of 18.2 (range: 7.3–44.1). Of those 13 children, 10 had an obstructive apnea index less than one (median of 0.1, range: 0–0.4) post AD/TC surgery. These 10 children were kept for the study of sleep characteristics. From these 10 children, only 8 children had polysomnographic recordings that were technically acceptable for spectral analysis of the heart rate. Statistical analysis was performed using Wilcoxon matched pairs test. AD/TC surgery was associated with a significant decrease in the number of micro- arousals during the night, as well as a decrease in the variability of the heart rate. The LFN values were significantly increased in all phases of sleep, while the HFN values were significantly decreased in all phases of sleep. The LF/HF values were significantly increased in all phases of sleep post-AD/TC surgery. The heart rhythm was significantly lower post-AD/TC surgery.

**Conclusions:** The surgical treatment of OSAS for children less than 3 years of age results in more restful nights and a lowering in nighttime autonomic activity. These findings support previously published data that obstructive apneas are associated with a disturbance of the autonomic nervous balance, and indicate that surgical treatment of OSAS can be beneficial even at a relatively young age.

**P 137**

**Idiopathic chronic sleep onset insomnia in Attention-Deficit/Hyperactivity Disorder: a circadian rhythm sleep disorder**

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**Objective:** To compare sleep-wake rhythm and dim light melatonin onset (DLMO) between ADHD children with chronic idiopathic sleep onset insomnia (SOI) and ADHD-and clinical controls without sleep problems.

**Methods:** 87 psychotropic-medication naïve children, aged 6-12 yrs., with rigorously diagnosed ADHD and SOI (ADHD-SOI), 33 children with ADHD without SOI (ADHD-noSOI), and 22 clinical controls were studied. One-week actigraphically measured sleep-wake rhythm, and DLMO measured from saliva were measured.

**Results:** Mean sleep onset in ADHD-SOI (21:38 ± 0.54 h (SD)) was significantly later than in ADHD-noSOI (20:49 ± 0.49 h; \( P < .001 \)) and clinical controls (20:55 ± 0.37 h; \( P = .05 \)). DLMO was significantly later in ADHD-SOI (20:32 ± 0.55 h) as compared to ADHD-noSOI (19:47 ± 0.49 h; \( P < .001 \)) and clinical controls (20:01 ± 1:02 h; \( P = .04 \)). Wake up time in ADHD-SOI was only later as compared to ADHD-noSOI (\( P = .002 \)), but not compared to the clinical controls.

**Conclusions:** Children with ADHD and chronic idiopathic sleep onset insomnia show a delayed sleep phase and a delayed dim light melatonin onset as compared to controls. This suggests they suffer from the delayed sleep phase syndrome.
Lack of association of ADHD-related chronic sleep onset insomnia and sleep hygiene level

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Objective: To compare sleep hygiene in ADHD children with chronic sleep onset insomnia (SOI) with sleep hygiene in ADHD children with normal sleep.

Methods: Participants were 74 medication naïve children, aged 6–12 yrs, with rigorously diagnosed and ADHD and SOI (ADHD-SOI), and 23 ADHD controls without sleep problems (ADHD-noSOI). Between-group differences were analyzed of lights out (sleep log), actigraphically evaluated sleep onset,-latency, and total sleep duration; and sleep hygiene as measured with the Children’s Sleep Hygiene Scale.

Results: We found a significant difference (p < 0.001) in mean (± SD) sleep onset between the ADHD-SOI group (21:49 ± 0.56 h) and ADHD-noSOI group (20:41 ± 0.45 h). Sleep latency was significantly (p < 0.001) longer in ADHD-SOI (0:53 ± 0:25 h) as compared to ADHD-noSOI (0:26 ± 0.25 h), and the difference of total sleep duration in ADHD-SOI (9:42 ± 0.44 h) and ADHD-noSOI (10:09 ± 0:43 h) was not significantly different (p = 0.18). Mean (± SD) TSHI scores in the ADHD-SOI group (56.4 ± 10.5) and ADHD-noSOI group (53.0 ± 10.6) did not differ significantly (p = 0.17).

Conclusions: There are no differences in sleep hygiene between ADHD children with chronic sleep onset insomnia and ADHD children with normal sleep.

The orthodontic approach in OSAS children: role of rapid maxillary expansion

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Obstructive Sleep Apnea Syndrome (OSAS) in children is characterized by prolonged partial or intermittent complete upper-airway obstruction, which affects normal ventilation during sleep. Both anatomic and neuromotor mechanism are considered to play a role in OSAS. The prevalence is 2.5% in children and is associated with high degree of morbidity, including growth retardation, neurobehavioural disorders, and cardiovascular complications.

In children, aged 2 to 8 years, the primary anatomic cause for OSAS is adenotonsillar hypertrophy, although abnormalities in the development of the lower-face skeleton have also been suggested. Guilleminault well described the craniofacial dysmorphism that leads to OSAS may involve a delayed growth of the mandible, producing the mandibular retroposition commonly found in patients with OSAS. Mandibular retroposition is associated with posterior displacement of the tongue base; this narrows the upper airway, predisposing it to collapse and contributing to the development of OSAS. A high arched palate is also common in patients with OSAS because the posterior tongue displacement may force the lateral palatine processes to expand over the abnormally placed tongue before fusing at the midline.

The most common approach in OSAS children is adenotonsillectomy, but it is limited by surgical risks and by recurrence. Children with OSAS are at risk for respiratory compromise postoperatively, due to upper airway edema, increased secretions, respiratory depression secondary to analgesic and anesthetic agents, and postobstructive pulmonary edema (1). Postoperative respiratory compromise has been reported to occur in 16–27% of children with OSAS. Particularly high-risk children include those younger than 3 yr of age, those with severe OSAS, and those with additional medical conditions (2); these patients should not undergo outpatient surgery. Postoperative polysomnograms 6–8 wk following surgery are recommended for patients with additional risk factors for OSAS, or those with a high apnea index, to ensure that additional treatment.

Guilleminault and colleagues reported a cohort of OSAS children treated by adenotonsillectomy, that developed a recurrence during adolescence (3). Thus, it appears that childhood OSAS is a dynamic process resulting from a combination of structural and neuromotor abnormalities, rather than from structural abnormalities alone.

Additional treatment options are available for those children who do not respond to T&A, or the small minority in whom T&A is contraindicated. Nasal CPAP is not approved by the Federal Drug Administration for children weighing less than 30 kg. Nevertheless, it has now been reported to be both effective and well-tolerated in hundreds of infants and older children (4), with side effects similar to those seen in adults. Nonetheless, the institution of CPAP therapy in young or developmentally delayed children can be challenging. Developmentally appropriate behavioral techniques are necessary for it to be successful. Another limiting factor is the lack of adequate pediatric interfaces and other equipment designed for children. For example, young or weak children frequently do not trigger bilevel ventilators. There is also concern among pediatric practitioners that the current nasal masks can cause midfacial depression when used in very young patients, for long time.

A useful alternative therapy for patients with sleep-disordered breathing, currently studied only in adults, is the...
use of an oral appliance. Despite their varying designs and mechanisms of action, advancing the mandible or the tongue or both, all these appliances induce their therapeutic effect by enlarging the upper airway (5).

Recently the orthodontic approach was evaluated in a controlled study of an Oral Jaw-Positioning Appliance (6) in 32 OSAS children (mean age 7.1 ± 2.6 yr; 20 males) presenting jaw deviation from normal occlusion: deep bite, retrusive bite and crossbite. 19 subjects were randomly assigned to undergo a 6-mo trial of a personalized oral appliance, the remaining 13 acted as a control and did not undergo therapy. The therapeutic rationale was that all orthodontic anomalies (except Class III) benefit from mandibular advancement capable of enlarging the retrolingual space and at the same time promoting lingual advancement The respiratory symptoms in all patients improved and in 50% of patients completely regressed (score = 0), where in control untreated subjects remained unchanged. Polysomnograms obtained after 6-mo trial showed that in treated children the A1 (Apnea Index) and AHI (Apnea-Hypopnea Index) were significantly lower after the trial (p < 0.001), whereas in control children both respiratory variables remained unchanged. Rapid Maxillary Expansion (RME) also plays a role in children with nasal breathing, OSAS and orthodontic problems. RME results in maxillary widening by distraction osteogenesis. A child can withstand up to 1 mm of expansion daily, but the speed of expansion varies. Radiographs of the region clearly indicate that RME moves nasal and palatal bones with a resulting increase in the nasal cavity width (7), lowering of the palatal vault, and straightening of the nasal septum with an improvement in nasal airflow recorded using acoustic rhinometry (AR) (8). Pirelli P. et al (9) demonstrated the therapeutic effect of the RME in 31 children (mean age 8.7 ± 1.9 yr; 19 males) with OSAS and maxillary contraction. The RME was kept in place from 6 to 12 months. The polysomnographic evaluations after the trial showed a AHI of less 1 event per hour in all cases (p = 0.46) and an impact on nasal cavities with a mean increase of the nasal pyriform opening of 1.3 ± 0.3 mm.


Mental disorders/Psychiatric/Personality

P 140
Effect of agomelatine on the sleep EEG in patients with Major Depressive Disorder (MMD)

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Introduction: Agomelatine is the first melatonergic antidepressant presenting an innovative pharmacological profile: melanin receptors agonist with 5-HT2C antagonist properties. Agomelatine 25 mg per day is effective in Major Depressive Disorder (MDD) without sedative or daytime drowsiness effects.1 The purpose of the study was to assess if agomelatine 25 mg induces specific effects on sleep architecture in outpatients suffering from MMD.

Methods: This open study involved 20 to 56 years outpatients with a new major depression episode (DSM-IV with baseline HAM-D score ≥ 20. Patients received agomelatine 25 mg/day p.o. for 42 days. Polysomnography and subjective evaluations were performed at D-1 (adaptation night), D0, D7, D41 (adaptation night) and D42. Recordings were performed with computerized sleep system with a 100 Hz sampling rate per channel, and included: EEGs (C3-A2, C4-A1, C3-O2), EOGs and EMG. Wake and sleep staging were analysed by international criteria (Rechtschaffen and Kales) and quantitative EEG analysis was performed with the PRANA software (PhiTools, Strasbourg). EEG power spectral analysis was performed on successive 2-sec window using a FFT algorithm with previous artefact rejection. Artefacts were detected by combining digital filtering and signal-dependent amplitude thresholds with subsequent review by expert. The delta ratio was calculated as follows: delta power first sleep cycle/delta power second sleep cycle. Patient’s subjective sleep perception was measured with the Leeds Subjective Scale.

Results: 15 patients (8 women), mean age 36 ± 11.3 years, were included in the study. Patients had a mean of 2.3 ± 1.1 previous MDD episodes. The HAM-D 17 item score was 21.8 ± 1.5. After 42 days of treatment the HAM-D 17 item score decreased to a mean score of 9.2 ± 5.5. The sleep efficiency (TTS/TSP * 100) increased by 4% (95% CI: 0.03-8.69), and the wake after sleep onset decreased from 42 to 19 minutes. Slow wave sleep (stages 3 and 4) increased by 16 minutes (95% CI: 1.79-26.06) with an increase of 4% of the total sleep period (95% CI: 0.69-6.28). Median time of sleep onset advanced from 00 h 03 to 23 h 37, and median time of minimum heart rate advanced from 05 h 10 to 04 h 34 (95% CI: -2:42-5:14). Delta ratio presented a trend to increase (from 0.93 to 1.3; 95% CI -0.06-0.62). Subjectively, “sleep quality” and “easiness falling asleep” improved on Leeds Subjective Scale from day 7 on. No effect was seen in different REM sleep indices.

Conclusion: This pilot study shows that agomelatine 25 mg at night time improved sleep continuity and quality in depressed patients. It normalized the distribution of SWS throughout the night. After only seven days of treatment, an effect on sleep quality was perceived by patients. Furthermore, agomelatine advanced the time of sleep onset, and the time of minimum heart rate suggesting a circadian effect.


Sleep in other medical disorders

P 141
Obstructive sleep apnea syndrome reflects a state of increased arterial stiffness in newly diagnosed essential hypertensive subjects
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Aim: obstructive sleep apnea syndrome (OSAS) may be involved in the pathophysiology of cardiovascular diseases through several mechanisms. Also, aortic stiffness seems to be an independent predictor of adverse cardiovascular prognosis in various clinical settings. We assessed the hypothesis that arterial stiffness is increased in untreated essential hypertensives (EH) with OSAS compared to a control hypertensive group.

Methods: we studied 46 consecutive subjects (35 men, aged 49 ± 8 years, BMI of 30.9 ± 3 Kg/m2, 24 smokers) with stage I, II untreated EH [office blood pressure (BP) = 150 ± 12/98 ± 9 mmHg] and OSAS diagnosed by polysomnography (PSG) [apnea/hypopnea index (AHI) > 5] and a control group of 53 untreated essential hypertensive subjects matched for age, sex, BP, smoking status and BMI with negative PSG. All subjects underwent echocardiography test to assess left ventricular mass index (LVMI) and relative wall thickness (RWT) and aortic pulse wave velocity (PWV) measurement by a computerized automatic device (Complior SP) and finally a full lipid profile and an homocysteine (HC) determination was performed as well.

Results: OSAS hypertensive group compared to hypertensive controls demonstrated similar levels of cholesterol (226 ± 40 vs. 228 ± 35 mg/dl, p = NS), while HC levels were higher in the OSAS group (14.27 ± 3 vs. 11.3 ± 4 micromol/l, p < 0.001). LVMI was similar in the two groups (109 ± 21 vs. 103 ± 23 gr/m2, p = NS), while RWT presented with greater values in the OSAS group (0.47 ± 0.06 vs. 0.42 ± 0.06, p = 0.01). Furthermore, PWV was greater in the OSAS hypertensives (8.56 ± 0.49 vs. 7.85 ± 0.93, p < 0.001). Within the OSAS group, PWV was correlated to age (r = 0.35, p < 0.05) and office systolic BP (r = 0.33, p < 0.05), but was not correlated to AHI (p = NS).

Conclusions: OSAS essential hypertensive subjects presented increased arterial stiffness compared to hypertensives without OSAS. The severity of OSAS was not correlated to increased arterial stiffness. Our findings may explain the possible more pronounced impairment of great vessels elastic properties in newly diagnosed essential hypertensive subjects with OSAS.

P 142
Normal CSF Hypocretin-1 levels in patients with huntington’s disease

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Aim: Huntington’s Disease (HD) is an autosomal dominant disorder with progressive movement disturbances, psychiatric symptoms, and cognitive decline. The underlying pathology is prominent neuronal loss in the basal ganglia. HD is often associated with sleep-wake disturbances [1] and with alteration in feeding behavior [2]. Hypocretin deficiency is the neurochemical hallmark of narcolepsy-catalepsy, a hypersomnia disorder which is related to altered food intake and obesity [3]. Recently, a marked loss of hypocretin neurons was shown in a mouse model of HD [4]. We therefore aimed to test whether CSF hypocretin-1 levels may be decreased in human HD.

Methods: CSF hypocretin-1 levels were determined in four patients with genetically confirmed HD, and in 3 patients with a HD-like disorder and negative genetic testing. Results were compared to 20 healthy controls.

Results: In all HD and HD-like patients, CSF hypocretin-1 levels were within normal range (mean 378 pg/ml; range
326-423; SD 37). There were no differences between HD and HD-like patients.

Conclusions: Our results indicate that hypocretin neurotransmission as assessed by determination of CSF levels is normal in HD, a disorder with neuronal death in select brain regions and changed sleep patterns.


P 143

Evolution of sleep apnea and blood pressure after acute ischemic stroke: a 3 months follow-up

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Background: The aims of our study are to determine (1) the evolution of sleep apnea (SA) severity/character (obstructive vs. central) and (2) the evolution of blood pressure (BP) after acute ischemic stroke, 3) whether severity and character of SA in the acute phase of stroke may affect BP evolution and clinical stroke outcome.

Methods: We studied 20 consecutive patients presenting within 96 hours after ischemic stroke onset to our stroke unit. Clinical evolution was monitored using NIH stroke scale and Scandinavian stroke scale on admission and 30 days thereafter (9±11/h). CAI was significantly higher acutely (CAI 8±12) than after 3 months (CAI 1±1) and 13 (65%) of 20 patients showed central apneas acutely compared to only 16% (3/19) 3 months later. (2) Systolic and diastolic BP values were significantly higher during night (p=0.001) and day (p≤0.001) in the acute phase (140±29/83±12 mmHg night, 151±24/95±16 mmHg day) compared to 3 months later (115±15/71±9 mmHg night, 128±12/81±7 mmHg day), despite no significant change in the antihypertensive treatment. (3) Blood pressure values in the acute phase, and therefore the extent of the BP decrease after 3 months, correlated significantly with the initial OAI, but not with AHI, CAI or change of antihypertensive medication. Higher systolic and diastolic BP in the acute phase correlated significantly with a worse functional outcome (higher mRS) after 3 months.

Conclusions: Elevated AHI in stroke is mainly due to increased number of central apneic events, which normalize within a time course of 3 months and seem to be rather a stroke-related phenomenon. The frequently observed decrease of BP values 3 months after stroke occurred independently of SA severity, CAI and clinical evolution. However, higher BP in the acute phase was linked to the presence of obstructive apneas at that time and to a worse clinical outcome after 3 months. Therefore, a differentiation of SA character in the acute stroke phase may provide helpful information about clinical evolution and outcome.

P 144

Sleep apnoea syndrome in acromegalic patients after therapy with octreotide

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Aims: To evaluate the relationship among biochemical activity, sleep apnoea severity parameters in a group of acromegalic patients and the effect of octreotide, a somatostatin analogue, on these indexes.

Methods: Ten patients with active acromegaly (age ± S.D. 48.7±9.3; 5M, 5F) were enrolled in the study. At baseline (T0), they underwent overnight polysomnographic evaluation and were reassessed after 8-12 months of treatments with octreotide (T1). Biochemical activity of the disease was assessed evaluating with levels of GH and IGF-1.

Results: At baseline assessment, 40% of acromegalic patients (4/10) had sleep apnoea syndrome (apnoea-hypopnea index, AHI >5) and 30% (3/10) presented a severe SAS (AHI >15). After treatment, there were significant improvements in hormonal profile and SAS parameters such as AHI (T0 vs T1, 23.1±30.3 vs 10±17.7, p <.05), lowest values of oxigen saturation (T0 vs T1, 83,
3 ± 18.7 vs 89.0 ± 17.9 p < .05) and arousal index (T0 vs T1 23.2 ± 15.6 vs 15.0 ± 9.6 p < .01). Moreover, there was a tendency towards a reduction in wake after sleep onset, an increase of sleep efficiency and an increase in the percentage of 3-4 NREM sleep and REM sleep. At follow-up, 30% of acromegalic patients presented still AHI > 5 and were addressed to CPAP therapy, but only one patient (10%) presented a severe SAS without normalization of hormonal parameters.

**Conclusion:** Our study confirm the high prevalence of sleep apnea syndrome in acromegalic patients and suggest that therapy with octreotide can improve also SAS parameters. SAS represents a well-known risk for post-operative management and it may be advisable to screen for SAS in acromegaly and consider preoperative treatment with octreotide in those with severe SAS.

**P 145**

Sleep Apnea before and after Cardiac Pacing for Sick Sinus

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**Objectives:** Atrial overdrive in sleep apnea patients with cardio pacemakers for sinus node dysfunction has been associated with a significant increase in both central and obstructive apneas. Such decrease in apneas and hypopneas has not been seen previously and mechanism behind it unknown. The aim of this ongoing study is to reveal the effect of standard pacemaker treatment on sick sinus syndromes in consecutive patients also evaluated for apneas and hypopneas. Further to study the effect of atrial overdrive on this patients category. Our objective is to verify previous results and to evaluate this group of patients further.

**Methods:** This is an ongoing prospective study. The target population are all Icelanders (total pop 290,000) needing a permanent dual-chamber pacemaker for sick sinus syndrome. When a decision about pacemaker has been made the patients are invited to participate by undergoing a sleep study and they are evaluated again 3 months postoperatively. Patients previously diagnosed with sleep apnea and those who are unwilling to participate are excluded. The patients undergo a whole night study with Embletta (Medcare, Iceland) a portable device for diagnosing sleep disordered breathing, which includes a single ECG channel. The pacemaker programming is standard.

**Results:** So far altogether 21 patients have been enrolled since October 1st, 2003 and 17 of them have already completed the follow-up study: 3 females and 14 males, mean age 74.8 years. The number of apneas and hypopneas per hour of estimated sleep (AHI) is shown in the Figure 1.

**Conclusions:** Our preliminary results in this ongoing study show only a small tendency towards a lower number of apneas and hypopneas following standard pacemaker treatment. Further evaluation to enlighten possible mechanism behind this change is ongoing. Might in future non-compliant CPAP treated OSAS patients benefit from pacemaker treatment with atrial overdrive.

**P 146**

Daytime Sleepiness and Fatigue in Relapsing Remitting Multiple Sclerosis (RRMS) during 24-Month Therapy with Interferon beta 1a

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**Introduction:** Fatigue and daytime sleepiness are common complaints in patients with multiple sclerosis. Amantadine and modafinil are often used for therapy. In clinical trials the Expanded disability Status Scale (EDSS) assesses disability. The NMSS Task Force introduced the MS Functional Composite (MSFC). The present study investigates the influence of the disease modifying drug interferon β 1a (AVONEX®) on fatigue, sleepiness, physical and cognitive functions measured by different scales in RRMS.

**Patients and Methods:** 24 patients with RRMS (11 men, 13 women, age: 34.1 ± 9.6 years) and 22 healthy controls (4 men, 18 women, age: 27.6 ± 5.2 years) were investigated with the following instruments:

**Extended Disability Status Scale (EDSS)**

MS Functional Composite (MSFC): ambulation (Timed 25 Foot Walk, T25W), arm function (9 Hole Peg test, 9 HPT) and cognitive function (Paced Auditory Serial Addition Test, PASAT) were investigated. The number of correct sums given in the PASAT (out of 60 possible), the mean time in seconds of two T25W trials and the mean time in seconds across four 9HPT trials (two with the dominant and two with the non-dominant hand) were used for analysis. Fatigue Severity Scale (FSS by Krupp et al.)
Estimation of fatigue in various situations with severity from 1 to 7

Epworth Sleepiness Scale (ESS)
Morning Questionnaire (DGSM)

First investigations were done before interferon-therapy. Patients and controls underwent follow-up after 6, 12, 18 and 24 months. Statistical analysis was performed by t-test for paired groups, Mann-Whitney-U-test for unpaired groups comparing patients and controls and the Spearman rank correlation coefficient.

Results: EDSS declined significantly after 12 months (1.7 ± 1.0 vs. 0.6 ± 0.9, p < 0.012) and afterwards rose again (1.4 ± 1.9). (No significant difference before and after 24 months of therapy). PASAT results rose after 12 months (40.8 ± 13.2 vs. 45.4 ± 14.5) and continued to improve (40.8 ± 13.2 vs. 50.9 ± 8.4 after 24 months, p < 0.03). Score of the Fatigue Severity Scale declined only in patients (32.2 ± 12.6 before vs. 28.1 ± 14.2 12 months vs. 30.6 ± 17.4 24 months). Epworth Sleepiness Scale in MS patients declined after 24 months (6.7 ± 3.5 beginning vs. 5.5 ± 3.3). Sleep Recreational Value improves after 24 months therapy (3.1 ± 1.1 vs. 2.3 ± 1.0). After 24 months of treatment FSS correlated with improved ambulation (T25W, r: 0.8, p < 0.05).

Conclusion: Fatigue occurs in up to 80% of MS patients. Therapy is mainly symptomatic. Though interferon β 1a may worsen fatigue during the first applications the present study demonstrates an improvement of fatigue and sleepiness over 24 months of therapy. Disease course stabilises as shown by EDSS and MSFC-results. As Fatigue improvement correlated to MSFC results this symptom seems to be related to demyelinisation. Interferon β 1a should also be considered for causal treatment of fatigue in MS.

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P 147
Actigraphy Estimated Sleep and Influencing Factors in Patients Undergoing Heart Surgery

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Aims: This study used sleep diary and actigraphy to investigate sleep in patients undergoing CABG or valve replacement surgery. Influencing factors included physiological, psychological, and environmental factors on sleep were also examined.

Methods: Nineteen patients (9 females, 10 males, mean ages 52.6 ± 10.8 years) wore Actiwatch (Mini Mitter, Oregon, USA) and filled out sleep diary on the third to the fifth post-operative days in ward. Physiological factors including fatigue, pain, and apnea, and environmental factors including light and noise were also assessed every day. The Pittsburg Sleep Quality Index (PSQI) was used to evaluate habitual sleep quality one month prior to heart surgery. The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression status before and after surgery.

Results: There were 73.7% of subjects complained about sleep disturbances before surgery (PSQI score > 5) with a mean global PSQI score of 7.63 (SD = 4.07). Actigraphic sleep efficiencies were decreasing (74.6%, 71.8%, 71.0%) and sleep latencies were increasing (24.9, 28.5, 33.7 min) during the third to the fifth post-operative days in ward. Patients with sleep disturbances prior to surgery had higher sleep efficiency (F = 5.54, p = 0.03) and longer sleep time (F = 8.56, p = 0.009) after surgery. Disturbed light during sleep was associated with longer awake time (r = 0.42, p = 0.05). Higher fatigue before sleep was associated with shorter sleep latency (r = −0.45, p = 0.04). Taking sleeping pills made no differences on sleep. Toilet (34.5%), noise (29.6%), and medical procedure (22.2%) were the main reasons to wake patients up in ward.

Conclusions: Sleep is disturbed in heart surgery patients during the third to the fifth post-operative days in ward. Previous sleep and environmental factors in ward affect sleep. Intervention in improving sleep in patients undergoing heart surgery should focus on adjusting the environmental factors.

P 148
Role of sleep-disordered breathing in patients with chronic heart failure

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Aims: Sleep-disordered breathing may adversely affect heart function, and thereby contribute to the progression of heart failure. A study was undertaken in patients with chronic heart failure (CHF) to document the characteristics of sleep-disordered breathing.

Methods: Forty-five patients with a diagnosis of CHF, comprising 25 patients with coronary artery disease (CAD) and 20 patients with essential hypertension (EH), underwent overnight polysomnography.

Results: Of these patients, 18 (72%) of the CAD patients and 11 (55%) of the EH patients had sleep-disordered breathing. Central sleep apnea-hypopnea syndrome (CSAHS) was seen in 12 CAD patients, but not in the EH patients, and obstructive sleep apnea-hypopnea syndrome (OSAHS) was seen in 7 CAD patients and 8 EH patients. CSAHS was seen in CAD
patients with a low left ventricular ejection fraction. EH patients with OSAHS had a significantly greater body mass index (BMI) than those without OSAHS and CSAHS (28.1 ± 3.5 vs 21.4 ± 3.8 kg/m², p < 0.05). CAD patients with OSAHS had a larger BMI than those with CSAHS (28.7 ± 5.2 vs 23.4 ± 3.6 kg/m², p < 0.05) and those without OSAHS and CSAHS (28.5 ± 4.9 vs 22.0 ± 2.8 kg/m², p < 0.05).

Conclusions: Sleep-disordered breathing is common in patients with CHF; almost half of CAD patients had CSAHS, which was closely associated with obesity.

P 149
Dream recall and instability of NREM sleep in a patient with right occipital artery infarction and antiphospholipid disease
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Introduction: Recalling dream is a brain process. The term Charcot-Wilbrand syndrome (CWS) is a cessation of dreaming following focal brain damage together the normal REM sleep architecture.1 However, patients with chronic stroke generally have normal sleep efficiency.2 Cyclic alternating pattern (CAP) has been described as a marker of instability of NREM sleep.

Objective: to evaluate CAP during NREM sleep and dream recall recordings in-patient with history of stroke at least 10 years before the sleep.

Methodology: A 42 years-old woman reported a total recalling dream loss, and she believed that had not dream capacity. She had diagnostic of antiphospholipid disease and right occipital artery infarction. This protocol performed seven-night polysomnography studies with intervals of 1 week. The patient was awakening for questions about dreaming activity after 10 minutes of REM sleep. Sleep was scored according to the Rechtschaffen and Kales criteria, adding CAP analysis in NREM sleep, according to the CAP atlas description.

Results: After this longitudinal study in sleep laboratory, the patient reported a better sleep pattern. The experimental interruption of REM sleep showed just two recalled dreams in 3th and 5th night of this protocol. The 5th-night-study was selected for CAP analysis. Sleep conventional variables is showed in table1. CAP rate was higher than normative data (75.3% versus 37.5%),2 also increase of CAP-phase-A2+phase-A3 (89.6% versus 40%)2. However, this patient have an important decrease in subtype of CAP-phase-A1 (10.4% versus 60%),2 that can be correlated with decrease in sleep-protective factors.

Conclusion: Patients with abnormal dream recall may also present abnormal NREM sleep, the relationship between the absence of dream recall and the NREM sleep disturbance will need further evaluation.

Table 1a

<table>
<thead>
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<th>Variable</th>
<th>Our patient</th>
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<td>SL (min)</td>
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<td>SE (%)</td>
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<td>REM latency (min)</td>
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3SL, sleep latency; total sleep time, TST; WASO, wake after sleep onset; ES, sleep efficiency; S1, stage 1 NREM; S2, stage 2 NREM; S3, stage 3 NREM; S4, stage 4 NREM.

P 150
Obstructive sleep Apnea Syndrome and Nocturnal Angina Episodes
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Objective: Study the relationship between obstructive sleep apnea syndrome (OSAS) and nocturnal angina of coronal heart disease (CHD).

Methods: Fifteen patients with CHD were admitted due to frequency nocturnal angina episodes. Nitroglycerin and Isosorbide Dinitrate to treat these patients without positive effects. Then all fifteen patients were confirmed severe OSAS(AHI > 30, SaO2 < 80%) by nocturnal Polysomnograms. Fourteen patients were treated with nCPAP (8–12 cmH2O) and one with nBiPAP(IPAP 14 cmH2O, EPAP 9 cmH2O).

Result: All clinical symptoms improved remarkably with the treatment. No heart angina occured again. Nocturnal myocardial ischemia improved significant with Holter of ECG Parameters of PSG changed as follows: Sleep efficiency decreased from 66 ± 13 to 90 ± 7, NREM/I/IST(%)(%) decreased from 92 ± 8 to 85 ± 9, stage I/TST (%) dropped from 72 ± 9 to 30 ± 14, stage ?+?/TST(%) risen from 5 ± 5 to 15 ± 6. REM/TST(%) increased from 7 ± 7 to 16 ± 16, AHI decreased from 70 ± 20 to 3 ± 3, the lowest SaO2(%) changed from 70 ± 10 to 90 ± 4.

Conclusion: There are great relationships between obstructive sleep apnea and ischemia heart disease. nCPAP can eliminated sleep apnea and improve nocturnal angina episodes.
P 151
Occurrence of gastro-esophageal reflux in patients with obstructive sleep apnea

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Aims: To evaluate gastro-esophageal reflux (GER) features both in OSAS patients and in control subjects respectively.

Methods: Fourteen patients with GER symptoms were included in the study. A simultaneous standard polysomnographic study and a 24-hour esophageal PH-metry were performed on each patient. OSAS was observed in 5 cases (5 M; age 54.2 ± 10.2; mean BMI 28.9; mean RDI 61.9) whereas 9 patients (5 M, 4 F; age 51.2 ± 9; mean BMI 28.4; mean RDI 2.7) were considered as controls. The following PH-metric parameters were studied: mean number of total and nocturnal GER episodes, mean nocturnal GER duration, acid exposure time (AET), De Meester Index (DMI).

Results: In OSAS group, a mean number of total GER events of 51.4 and a mean DMI of 16.4 were observed, while control group had a mean number of total GER events of 59.11 and a mean DMI of 11.2. Nocturnal AET was significantly different in the two groups (OSAS vs non OSAS 3.9% vs 1%, p = .05). Nocturnal GER episodes occurred mostly during 1-2 NREM sleep in OSAS patients, while mainly during wakefulness in controls. In OSAS patients, 45.4% of reflux events were preceded by arousal and 46.5% by apnea.

Conclusion: OSAS patients showed greater number of nocturnal GER episodes and greater severity of disease when compared to control subjects.

P 152
Questionnaire study on sleep disorders in stroke survivors

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Aim: The aim of the study was to assess the prevalence and intensity of sleep disorders in patients who have survived ischaemic stroke.

Methods: We have used the following sleep questionnaires: Soldatos Insomnia Scale, Epworth Sleepiness Scale, Sleep Disorders Questionnaire, Beck’s Depression Index. We have sent the questionnaires to subjects who were hospitalised in the Department of Adults’ Neurology, Medical University of Gdansk in years 2003 to 2004. The questionnaires were anonymous.

Results: We have sent 150 questionnaires and we have received 62 questionnaires, of which 53 were analysed (28 M, 25 F). The mean age of the group was 67.98 years. The mean result in the Soldatos Insomnia Scale was 17.2 points. The mean Epworth Sleepines Scale score was 9.16. The following symptoms developed in the patients after the stroke: restless legs (45.3% of the patients), periodic limb movements (30.2%); frequent awakenings (50.9%), sleep paralysis (28.3%), sleep-disordered breathing (33.9%), bruxism (15.1%), somnambulism (13.7%), nightmares (20.7%), sleep behaviour disorders (15.1%), uncontrolled daytime naps (41.5%). The mean score of the Beck’s Depression Index was 39 points.

Conclusion: Ischaemic stroke should be considered as a risk factor of developing multiple sleep disorders. Those disorders may lead to decrease of the patients quality of life and they may be correlated with depression. The analysis of the correlation of the brain lesion location and the type of sleep disorder may lead to a better understanding of the sleep mechanisms.

P 153
Influence of the severity of hepatic cirrhosis upon diurnal sleepiness and sleep parameters

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Aims: To assess a possible association between the severity of hepatic cirrhosis and both diurnal sleepiness and sleep parameters.

Methods: 42 patients with hepatic cirrhosis were prospectively assessed, being 33 males, aged 50.3 ± 8.4y. All the patients were evaluated by clinical assessment, liver function tests, Epworth Sleepiness Scale (ESS) and submitted to polysomnogram (PSG). The ESS and PSG data were compared with those of healthy controls, matched by age and sex. Patients were classified according to the prognostic model of CHILD-TURCOTTE-PUGH (CTP) in classes A (5-6 points), B (7-9 points) and C (10 or more points). Ten patients had already experienced overt hepatic encephalopathy. ESS scores and sleep parameters were compared among the 3 classes of CTP using ANOVA followed by Duncan test whenever necessary. The “t” test was used to compare the ESS scores and sleep parameters in cirrhotic patients who had and had not previous episodes of overt hepatic encephalopathy.

Results: There was a significant difference among CTP groups in regard to REM sleep percentage, significantly lower in group C in relation to groups A and B (ps < 0.002),
and REM latency, significantly higher in group C only in relation to group A (p=0.01). There was no difference between the 3 groups in regard to the ESS. However, the patients who had had previous episodes of overt hepatic encephalopathy presented significantly higher scores in ESS latency when compared to those without previous episodes (mean: 6.75 vs 10.70; p = 0.02).

Conclusion: The findings suggest that cirrhotic patients with more accentuate liver failure have lower REM sleep percentage and higher REM latency, and the patients who had experienced previous episodes of overt hepatic encephalopathy presented higher scores in ESS, with mild to moderate diurnal sleepiness.

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P 154
Sleep-Wake-Disorders after Traumatic Brain Injury: a Prospective Study

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Aims: Sleep-wake disorders are well known from clinical practice to complicate the course of traumatic brain injury. The aim of this prospective study is to assess their prevalence and characteristics.

Methods: Six months after traumatic brain injury (TBI), 53 consecutive patients (43 males, 10 females, mean age 37.2 years) were examined by means of sleep questionnaires, clinical examinations, computed tomography of the brain (CT), laboratory tests (including HLA typing, and cerebrospinal fluid hypocretin-1 determination), polysomnography (PSG, available in 48 patients), and multiple sleep latency tests (MSLT, available in 46 patients). Statistical analyses were performed by Pearson correlation tests, Mann-Whitney U-tests, student t-tests and paired-samples t-tests.

Results: 33 of 53 patients (62%) reported sleep-wake disturbances following TBI, whereas 29 out of 53 patients (55%) suffered from increased fatigue or excessive daytime sleepiness compared to before TBI. Epworth Sleepiness Scale (ESS) score was abnormal (> 10) in 14 of 53 patients (26%). ESS scores were significantly increased after TBI compared to pre-TBI conditions (p < 0.005). Increased night sleep time (≥ 1 hour more than pre-TBI) was reported in 14 patients (26%). One patient (2%) reported insomnia. Mean sleep efficiency on PSG was 82% (range 67.8–99.6), mean arousal index 8.0 (range 0.4–42.7). Sleep onset REM sleep (SOREM) on PSG was observed in three patients. Mean sleep latencies < 5 minutes were found in 12 of 46 (26%) patients (mean 8.0 minutes), and were significantly lower in patients with mild TBI (mean 7.9 minutes, SD 3.3) when compared to patients with moderate/severe TBI (mean 12.1 minutes, SD 4.5; p = 0.031), irrespective of apnea-hypopnea- or periodic limb movement indices. Four patients had ≥ 2 SOREM’s on MSLT, whereof only one patient had a mean sleep latency of < 5 minutes. Subjective estimation of sleep-wake disorders as well as PSG and MSLT findings were independent of severity or localisation of TBI, gender, age, pathological neurological findings, HLA typing, or hypocretin-1 levels (normal in all patients).

Conclusions: The prevalence of 62% in our study population shows that complaints of sleep-wake disorders are common after TBI. Excessive daytime sleepiness as assessed by sleep questionnaires and by multiple sleep latency tests is the most frequent sleep-wake disorder following TBI, whereas insomnia was reported only by one patient. Surprisingly, patients with mild TBI are more at risk to develop posttraumatic sleep-wake disorders. Other risk factors for the development of posttraumatic sleep-wake disorders such as demographic characteristics or HLA findings could not be identified, and correlations between localization of pathological CT findings, hypocretin levels and outcome were not found.

Sleep Health Care Delivery

P 155
Factors influencing quality of sleep in primary caregivers of patients with Alzheimer’s disease

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Aims: We surveyed patients with Alzheimer’s disease (AD) and their caregivers to validate factors that contribute to sleep disturbance among the caregivers.

Methods: Sixty-seven outpatients with diagnosis of AD and their primary caregivers were studied. Patients were assessed with Mini-Mental State Examination (MMSE) and Clinical Dementia Rating (CDR). Neuropsychiatric manifestation was ascertained using the Neuropsychiatric Inventory (NPI), and activities of daily living (ADL) was also evaluated. Sleep state of the patients was assessed by Sleep Health Risk Index (SHRI). Caregivers were checked about their caregiver burden and their own sleep state. The influential factors for sleep disturbance of caregivers were analyzed using stepwise multiple regression analysis.

Results: Of the 67 patients, 9 did not respond, 8 lived alone, and 8 stayed in nursing homes or hospitals. Finally, a total of 42 patients (12M/30W, 78.1 ± 6.7 years of age) were
included according to our inclusion criteria. Caregivers burden and sleep maintenance problems in patients were the variables which entered the regression equation for sleep disturbance in caregivers. Sleep fragmentation in patients was the strongest factor, followed by caregiver burden.

**Conclusions**: A significant relationship was observed between sleep state of caregivers and patients’ sleep maintenance problems. In addition, the degree of caregiver burden was also an important factor for sleep disturbance of caregivers. The maintenance of sleep quality should be taken into consideration in AD treatment because of the high prevalence of sleep disturbance in AD, which potentially affects sleep in their caregivers. Moreover, it is important to appreciate that sleep problems of caregivers are not necessarily correlated with the cognitive function of AD, which may indicate that even AD patients in the early stage could cause sleep disturbance in their caregivers.

**P 156**

**CPAP Compliance in Singaporean patients with Obstructive Sleep Apnoea**

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Continuous positive airway pressure (CPAP) is the gold standard form of therapy for patients with obstructive sleep apnoea. However, compliance is poor and treatment failure common.

A retrospective study involving twenty-five patients diagnosed with OSA who were subsequently started on a trail of CPAP therapy. Using the Respironics Remstar home CPAP device, patient compliance data was extracted after 1 month. This was then compared to the following factors, Age, sex, race, educational level, marital status, Epworth sleepiness score, apnoea-hypopnea index (AHI), lowest arterial saturation (LSAT) and cpap settings.

Using statistical analysis, high AHI, was the only statistically significant variable associated with higher CPAP compliance

**P 157**

**Assessment of the sleep disorder and confront methods of those in elderly persons**

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Sleep is one of the essential needs for human and every disorder in during of sleep causes psychological problem and decreased person’s ability. Although sleep disorder occur in ever of ages, elderly person usually has very problems for satisfied sleep. The aim of this study was to estimate prevalence of sleep disorders and confront methods of those in elderly persons.

This is a descriptive analytical research. 200 elderly residents of Semnan city were selected through randomize sampling. Sleep disorders was assessment by questioner and interviewer that include of sleep disorders (Insomnia, Parasomnia) and confront methods (behavioral, cognitive, sleep hygiene and drug therapy).

Data indicated that prevalence of all disorders were 97% (insomnia and Parasomnia) in all stages of sleep (early, middle and end). In the part of confront methods of sleep disorders, 57% used of behavioral therapy. The most of that (25%) were concentration of the limb before the sleep and 95.5% of them comprehension of cognitive methods. The most of that (36%) were comprehension of effect of age on sleep. 100% of them orientation of sleep hygiene and the most of that (39%) were orientation with 4 choose of sleep hygiene. 20% of them used of drug therapy.

Finding above indicated that prevalence of sleep disorders relative was high in elderly persons in Semnan area, that need supervised and widespread program for promoting awareness among population about sleep disorders and confront methods of those.

**P 158**

**Sleep Disorders in Rural Versus Urban Populations**

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**Aims**: There is a paucity of world-wide demographic data concerning the rates of sleep disorders (SDs). In the USA alone, an estimated 40 million people suffer from SDs, which are linked to numerous adverse health effects. Despite their prevalence, SDs remain inadequately reported, diagnosed, and understood. SDs are not only detrimental to an individual’s health (physical and psychological), but create tremendous negative societal burdens. Studies in the USA have found that rural residents are significantly less likely than those living in urban areas to obtain certain preventative health services, and are further behind in meeting the Healthy People 2010 national health promotion and disease prevention objectives. Rural residents may have different values than those in urban areas that contribute to seeking medical care only when seriously impaired by the health problem. Additionally, obesity, which is related to an increased risk for developing SDs, is more prevalent in rural populations, particularly those 25–44 years old and those over age 75. Comparisons of SDs and SD correlates such as
hypertension, stroke, obesity, depression, and heart failure, in rural and urban residents would facilitate a clearer understanding of health implications in these groups and may lead to better referral and treatment options.

Methods: We assembled an interdisciplinary team of professionals and constructed a 111-item questionnaire to assess sleep habits, sleep observations, past medical and psychological history, prior treatment approaches for SDs, social information, and medications. We used the questionnaires in conjunction with NP studies, multiple sleep latency tests (MSLT), the Epworth Sleepiness Scale (ESS), and medical chart reviews of people referred to our institution for evaluation of SDs. Participants were classified as living in rural, rural with urban access, or urban areas. Comparisons of symptoms, diagnoses and psychological and medical problems were made between groups.

Results: We compared data from 163 participants referred to our institution for evaluation of sleep problems. Of those, 131 were urban residents, 8 lived in rural areas with urban access, and 24 people lived in rural areas. A sample of findings included that those living in rural areas were significantly more likely to snore, fall asleep while driving, experience problems with memory and attention to detail, and to be obese than were their urban counterparts. Conversely, those living in urban areas were significantly more likely to have major concerns about their sleep and health.

Conclusions: Improved recognition of SDs is required world-wide. Factors such as urban versus rural domiciles and the health attitudes specific to those constructs need to be integrated into the equation to facilitate a better understanding of SD’s and their effects.

P 159
Incidence of complication of radiofrequency treatment of the palate and tongue base in OSA patients

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Radiofrequency therapy to the palate and tongue base is a convenient and an efficient modality for outpatient treatment of sleep disorders. However the complications are not well studied.

This is a retrospective study involving 58 patients who have undergone radiofrequency treatment of the tongue base and palate. They were subsequently followed up for three months and complications arising from the procedure were recorded. The complications were divided into minor (mucosa ulceration, crusting, and uvular sloughing), moderate (haemorrhage, fistulation and dysphagia) and severe (airway compromise). The incidence of complications were correlated with energy related and treatment duration.

In the three month period of study, there were only two patients with minor complications and one with moderate complications. This suggests that radiofrequency treatment is a safe modality for outpatient treatment of sleep disorders.

Epidemiology/Individual Differences

P 160
Quality of sleep of media personnel with or without irregular shift work

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Aims: The study was carried out to compare the objective and subjective data about sleep quantity and quality in media personnel in regular work and irregular shift work.

Methods: A wrist actigraph was held for a week by 86 employees of the Finnish Broadcasting Company with irregular shift work (40 men, 46 women) and 55 randomly selected controls (26 men, 29 women) in the same company with regular eight-hour daytime work. A sleep questionnaire and an SCL-90 questionnaire for psychological symptoms were filled.

Results: The average mean total sleep time of the employees with irregular shift work measured with actigraph was on weekdays 6.0 h and that of the controls 6.5 h (p = 0.009), subjectively 6.4 and 7.0 h, respectively (p = 0.006). Sleep efficiency was not significantly different between the groups. The percentage of immobility phases of one minute was 5.56 with shift work employees and 7.24 with controls (p = 0.025). According to logistic regression, the percentage of immobility phases of one minute was positively associated with subjective early morning awakenings (p = 0.018), difficulties initiating sleep (p = 0.026) and subjective symptoms of anxiety with regular daytime work employees but not with shift work employees.

Conclusions: The media personnel with irregular shift work slept less but their sleep was less fragmented, ie. somewhat better in quality. Subjective estimates and objective actigraphy data correlated well with daytime work employees but somewhat poorer with irregular shift work employees, probably because of their unusual rhythms of work, spare time and sleep.
Subjective and objective sleep quality in noncomplaining elderly subjects

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Introduction: Although aging is associated with significant changes in sleep, this does not necessarily result in complaints about sleep quality. It seems that in older adults sleep complaints are often secondary to other health problems and that healthy noncomplaining older individuals adapt their perception of what is “acceptable” in sleep. Here, the relationship between subjectively perceived sleep quality and objective measures of sleep is analysed in a sample of elderly subjects (60 to 82 years) who felt that they had no significant problems with their sleep (non-complaining subjects).

Methods: The present sample comprises 70 subjects (48.6% females), who all passed an intensive screening procedure to rule out significant physical or mental illnesses. The mean age was 65.6±4.7 years. Subjective sleep quality was assessed by means of the Pittsburgh Sleep Quality Index (PSQI). Objective data on sleep quality (sleep period time: SPT, total sleep time: TST, sleep efficiency index: SEI, sleep latency: SL, number of stage shifts, and amount of wake, stages 1, 2 and slow wave sleep of NREM sleep and REM sleep (in percent of SPT) resulted from polysomnographic recordings of the adaptation night spent in the sleep lab. For quantitative sleep variables, gender differences and differences between subjects with a PSQI score indicative (>5) and not indicative (≤5) of a disturbed sleep were tested by Kruskal-Wallis test with a double sided p<0.05.

Results: Overall the PSQI-scores ranged from 0 to 9 in males and from 0 to 12 in females. The mean PSQI-score was 4.3±2.4. There was no statistically significant gender difference in the distribution of the PSQI-scores. The number of subjects with PSQI-scores >5 (which indicates “poor” sleep) was 26.5% in females and 22.2% in males, again no statistically significant gender difference. Three of the sleep variables showed statistically significant gender differences: females had more slow wave sleep (11.3 vs. 4.7%; p<0.001), less NREM stage 1 sleep (15.4 vs. 19.7%, p=0.0197) and a longer REM sleep latency (94.7 vs. 73.7 min, p=0.0436). There was no statistically significant correlation between PSQI-scores and objective sleep parameters. Furthermore, objective sleep parameters of subjects with PSQI-scores indicative of a “poor” sleep did not differ significantly from those observed for subjects with PSQI-scores reflecting a non disturbed sleep. A logistic regression revealed that neither sleep parameters nor gender were statistically significant predictors of a PSQI-score >5.

Discussion: Our results do not support earlier findings by Vitiello et al. [2004] who observed a significantly impaired objective sleep with longer sleep latency, less total sleep time, and lower sleep efficiency in healthy men (but not women) with a PSQI-score >5.

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Knowledge, awareness and attitude of people to sleep related disorders. A hospital based pilot survey

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Aim: In India Sleep disorders is a relatively new and emerging field of medicine. Knowledge and awareness of sleep related problem among public and health care professionals is scanty. The aim of this study is to evaluate this aspect and consider future community based studies.

Material and Methods: 40 patients (32–64 yrs) and 60 normal subjects (20–67 yrs) were screened over the past 1 year using a standard questionnaire based proforma for sleep disorders and a 5 point questionnaire for awareness of sleep disorders.

Results: Among 40 patients (BMI-28.6±4.61) evaluated 37 had obstructive sleep apnoea (OSA)- Severe in 10, moderate in 10 and mild in 17. COPD was seen in 3 cases. The mean duration of symptoms was 5.98±4.10 years. Although CPAP was recommended, most patients opted for pharmacological and non pharmacological management (weight reduction avoidance of alcohol and smoking) because of high cost of the CPAP equipment. Most of 60 normal subjects evaluated considered snoring as normal and natural. 18%of the subjects snored during sleep and did not seek any medical attention. 12% had them selves or a relative suffering from lack of sleep for varying periods but never consulted a doctor. Public awareness on sleep related problems was poor as revealed in this study. GPs (general practioners) and physicians had no exposure to sleep disorders in their medical curriculum and could not recognize the problem and refer the patient to sleep specialists.

Conclusion: This short observation reveals that more public education through visual media and print and inclusion of sleep disorders in basic medical curriculum will increase the knowledge and awareness among all concerned.
Prevention of Ill-health Effects of Stress and Lifestyle (Part 21)-Relationship of Lifestyle, Stress, and Diurnal Preference

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Aims: To investigate the interactive effects among diurnal preference, lifestyle, and mental health status among workers in Japan.

Methods: A self-administered questionnaire survey was conducted among 242 male employees aged 19 to 62 years at the company of metalworking industry in Japan at 2003. The questionnaire consisted of the eight health practices recommended by Morimoto, the General Health Questionnaire-28 (GHQ-28), the Zung Self-rating Depression Scale (SDS), the Horne-Ostberg Morningness-Eveningness questionnaire (MEQ), and demographic variables. Odds ratio (OR) were calculated using chi-square test.

Results: The OR for the GHQ-28, the SDS, nutritional balance, and eating breakfast was 2.75 (95% confidence interval, 1.04–7.27), 3.32 (1.21–9.15), 3.81 (1.32–11.0), and 6.72 (2.47–18.3), respectively, in eveningness compared with others. Sleeping less than 7 hours and working less than 10 hours indicated significant OR in the SDS, nutritional balance, and eating breakfast in eveningness.

Conclusions: These results suggested that mental health status and dietary habits were affected by eveningness tendencies.

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P 165
Prevalence of Obstructive Sleep Apnea in Commercial Truck Drivers in Finland

Aim: To evaluate the prevalence of obstructive sleep apnea (OSA) in commercial truck drivers in Finland by a questionnaire and sleep laboratory studies.

Methods: A questionnaire was sent to a sample of 2066 commercial drivers in Southern Finland. A subsample of 75 responders (Group1) fulfilling criteria for possible OSA (habitual loud or irregular snoring for minimum of 20 years, witnessed apneas) was recruited for further studies in sleep laboratory. Also a control group of 72 subjects (Group2) with no snoring/apneas received a detailed evaluation by a nocturnal polygraphic recording (SaO2, airflow, breathing movements, pulse, sleeping position), and MWT on the following day.

Results: Response rate to the questionnaire, after contacting additionally 50 persons by telephone, was 53.2%. Mean age of the responders was 40.7 years (SD 11.0). Mean BMI in Group1 was 30.4 kg/m2 (SD 6.3) and in Group2 26.4 (SD 4.6), P < 0.001. Mean ESS for Group1 was 9.9 (SD 4.4) and for Group2 7.7 (SD 3.4), P < 0.005. AHI > 5 was found in 41.9% of the subjects tested in sleep laboratory, which gave an estimate of the prevalence of obstructive sleep apnea in commercial truck drivers in Finland.
OSA of 25.1% in the whole population. Mean sleep latency in MWT was 26.7 minutes (SD 11.8) in Group1, and 31.3 minutes (SD 9.4) in Group2 (P=0.01). The prevalence of OSA (AHI > 5) with problems staying awake in the MWT (mean SL < 19 min) was 7.9%.

Conclusions: The prevalence of OSA with increased sleepiness as witnessed by MWT is 7.9% among Finnish commercial truck drivers. The prevalence of OSA in general is 25%. Thus, OSA is common in truck drivers. It is important to know who of them are sleepy before prohibiting someone from driving. We are now using MWT and a long driving test by a real car in normal traffic prohibiting someone from driving. We are now using MWT and a long driving test by a real car in normal traffic.

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Sleepiness as a cause of fatal traffic accidents

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Aims: To study relationships between fatigue/sleepiness and fatal traffic accidents with at least one death.

Methods: The data is from the database of the Finnish Motor Insurers’ Centre (Traffic Safety Committee of Insurance Companies, VALT). The population consists of 4,563 death-related accidents between the years 1991–2000. All accidents have been carefully investigated by groups of experts in accident investigations. All seriously injured subjects have been medically examined, and deceased subjects have autopsies with measurements of blood glucose, alcohol and drugs. A smaller sample was collected from the fatal accidents that occurred in 2000 (N=514). New variables were added and all cases were reanalysed case by case to find probable and possible sleep-related accidents. Almost certain and possible sleepiness-related traffic accident were selected based on the reanalysis.

Results: In the official Finnish data 4.8-19% of traffic accidents are related to sleepiness. In this study the occurrence of probable sleep-related accidents was 31.5% (N=1440). In 96.3% of these the driver’s sleepiness and/or falling asleep at wheel was the reason for the accident. These were either single car accidents or the driver was interpreted as having caused the accident. Sleepiness-related accidents were most common during May-August (39.5% of accidents) and least common during January and February. Young drivers, aged < 25 y, were more prone to sleepiness-related accidents than older drivers. 57% of the sleepy drivers and 11% of the others had slept < 6 hours (P < 0.0001). In a multiple logistic regression analysis the strongest factors for a sleepiness-related fatal accidents, alcohol-related accidents excluded, were: (a) being awake for more than 21 hours (OR 1.59; 95% CI 1.14–2.23), (b) less than 6 hours of sleep (OR 1.45; 1.24–1.70), (c) driver’s age less than 26 years (OR 1.28; 1.16–1.41) and (d) driving between 01–06 a.m. (OR 1.09; 0.90–1.33; NS). When also alcohol was taken in the model the strongest factors were: (a) blood alcohol > 0.05% (OR 3.82; 2.83–5.16), (b) sleep < 6 h (OR 1.89; 1.34–2.64), (c) age < 26 y; (OR 1.45; 1.17–1.80), (d) male driver (protective; OR 0.51; 0.39–0.67), and (e) wakefulness > 21 h (OR 1.74; 0.87–3.47; NS). 15.5% of the professional drivers accidents were due to sleepiness or falling asleep at wheel. 85.7% of the professional drivers’ accidents occurred during work and 14.3% during leisure time or holidays.

Conclusions: Sleepiness related traffic accidents are common and sleepiness must always be considered as a possible cause for an accident especially if there is a some combinations of the following: (a) short sleep preceding the accident, (b) long wakefulness exceeding 21 hours, (c) an early morning hour, (d) history of some alcohol drinking with even low level of alcohol in the blood.

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Effects of awaking from REM and NREM sleep

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Aims: In the past, there was mostly anecdotal evidence that patients generally perceive their sleep as worse when they are awakened from REM sleep. The authors analysed parameters at awakening to identify whether there is any difference in levels of sleepiness, fatigue and dream recall dependant on terminal sleep stage.

Methods: A consecutive series of 100 patients was sampled for several key variables: general patient information including medication use, major PSG parameters (sleep efficiency and duration, sleep stage percentage, arousal index and last sleep stage before awakening) and a post-sleep query consisting of a 7-item Fatigue Scale, 7-item Stanford Sleepiness Scale and 4-item dream recall questionnaire. Patients were divided in to two groups, depending on their terminal sleep stage before awakening (NREM and REM sleep group).

Results: There was no major difference in general and PSG parameters, or levels of fatigue and sleepiness post awakening between these two groups. Statistically significant difference between groups was observed in a dream recall (p < 0.008**) and disturbing dream recall (p < 0.04*), in that the REM group had higher total recall of dreams (1.52 ± 1.31 v. 0.75 ± 1.35) and recall of disturbing dreams (0.59 ± 1.04 v. 0.2 ± 0.54). At the same time, this group had a higher average amount of REM sleep recorded. To assert that the amount of REM sleep is not determining dream recall, a subset from the NREM group with high REM percentage was extracted, and the same comparison was
made between the REM group and the high REM percentage NREM subgroup, which again showed a statistically significant difference between the (sub)groups in both the dream recall ($p<0.001^{***}$) and a disturbing dream recall ($p<0.02^*$). There was no major difference between REM and NREM groups in terms of the medication use, and in particular use of REM suppressing medication or medication that may augment disturbing dreams.

**Conclusions:** One of the reasons why patients may have negative perception of their sleep is higher level of (disturbing) dream recall when they are awakened from REM sleep. In a sleep laboratory setting, this fact may merit waiting for a patient to reach a consolidated NREM sleep before waking him up. The perception of fatigue and sleepiness upon awakening appears not to be determined by terminal sleep stage.

**P 168**  
**Short sleeper: a study of prevalence**

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**Introduction:** “Short sleeper” has been proposed as a sleep disorder. Since this nosological status does not have a solid foundation, it is important to assess the various aspects of this “category”. The prevalence of the condition is unknown, although it is considered to be “apparently rare” (ICSD, 1997). The aim of this study was to know the prevalence of “short sleeper” in a young adult sample.

**Methods:** The questionnaire includes: (1) socio-demographic information, (2) Sleep environment, (3) Sleep habits, (4) Horne & Ostberg Questionnaire (MEQ), (5) Sleep disorders, (6) Epworth Sleepiness Scale (ESS), (7) Life style, including physical activity, use of psychoactive drugs and eating habits, (8) Health status, (9) Academic performance, (10) Recent events and behavior. A decision tree (see Results section) was used to define short sleeper.

**Results:** The final prevalence of short sleeper was 3 subjects (0.24% of the total sample) after screening the whole sample according to the following steps: (1) Sleep duration of less than 6.5 hours on workdays; (2) Not to complain of insomnia or hypersomnia; (3) Not to have an ESS score higher than 10 and/or diurnal “sleep attacks”; (4) Not to miss classes due to sleep; (5) Not to fall asleep in class; (6) Not to sleep more on the weekends; (7) Not to complain about sleep quality, sleep depth and sleep restorative power; (8) Not to take long naps.

**Conclusions:** The condition of short sleeper appears to be extremely rare in young adulthood, an age in which the pattern is considered to begin.

**P 169**  
**Sleepy on the highway-a roadside study**

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**Aims:** Car-driving demands a high level of attention and concentration. At least 25% of accidents on German roads occur as a consequence of driver sleepiness. On the way to change this, a quantitative risk analysis about the hazards of sleepiness whilst driving is inevitable. For this purpose objective and handsome methods are needed.

**Methods:** PST: Central nervous activation was assessed by the Pupillographic Sleepiness Test (PST by AMTech, Weinheim, Germany) described elsewhere. This recording is performed in the sitting subject and lasts 11 minutes. PST recordings were performed in rooms of the road house and a container on the parking lot. Subjective sleepiness: Stanford Sleepiness Scale. Subjects were recruited on a voluntary base in summer 2004 while visiting the road house or taking a break on the parking lot. Measurements were completely anonymous. Subjects were asked about time at the wheel, time awake, caffeine and nicotine consumption and subjective sleepiness. Drivers received general informations about the risks of sleepiness whilst driving. After each recording we recommended countermeasures of sleepiness (power nap, caffeine) to those drivers showing extremely or suspected sleepy PST values.

**Analysis:** The natural logarithm of the Pupillary Unrest Index (lnPUI) was analysed and classified according to the reference values of the PST into three classes: normal (mean ± two SD) and suspected sleepy (between the others). Frequencies of sleepiness classification were determined and correlations were calculated according to Spearman concerning PST, subjective sleepiness and/or behavioural variables.

**Results/Discussion:** 63 drivers took part in the measurements. PUI was in the normal range in 43% of the group while 25% showed severe sleepiness. 32% were suspected for sleepiness. No significant correlations between tested variables were observed. While the percentage of sleepiness is in line with former studies, other projects have shown PUI-correlations to subjective sleepiness and/or behavioural variables. None of the heavily sleepy drivers’ group took the
chance of taking a nap in motel rooms which were freely available for this purpose.

**Conclusions**: Although there is a high interest in knowledge about their own sleepiness drivers hesitate to draw necessary consequences when sleepy.

**Acknowledgments**: This trial was sponsored by * Bayerisches Staatsministerium für Umwelt, Gesundheit und Verbraucherschutz, Referat 742 Arbeitsmedizin, Arbeitssicherheitsorganisation, München.*

**Instrumentation/Methodology**

**P 170**

A *Wake-REM-NREM Automatic Analysis Using a Single EEG Channel: Epoch by Epoch Comparison with Human Sleep Scoring in Healthy Subjects*

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**Aims**: Facing the increasing demand for diagnosis of sleep-associated pathologies, especially respiratory sleep breathing disorders, ambulatory polygraphy was developed. However, with such devices the apnea-hypopnea index is often underestimated due to the absence of concomitant sleep evaluation. We have developed an automatic analysis software able to detect sleep, based on single-channel EEG recording that could easily be integrated in an ambulatory device. The aim of this study was to validate the sleep scoring by our analysis software, compared to the manual analysis of conventional polysomnography.

**Methods**: ASEEGA (Automatic Sleep EEG Analysis) is an automatic software which provides the all-night hypnogram from a single EEG channel. This software is an extension of the seminal work of O. Benoit and J. Prado [1], who proposed a semi-automatic approach requiring a single EEG channel. This method has been successfully and routinely applied to more than 500 recordings (from both healthy subjects and patients) for more than 12 years (since 1984), including hypnotic pharmacological trials [2]. The method has been further improved into an automatic laboratory-recorded sleep EEG analysis [3]. Recent research and development work has resulted in the ASEEGA software, which is now able to analyze the EEG from signal obtained with recording devices that are routinely used in sleep centers. The ASEEGA unsupervised approach has the ability to distinguish between Wake and Sleep states, as well as between Wake, REM and NREM states. ASEEGA was evaluated on 15 healthy subjects (age: 29.2 ± 8.0 years). Each night recording was analyzed according to a triple blind procedure: one automatic analysis with ASEEGA based on the sole CzPz EEG channel and two separate visual analyses performed by two different experts (X.D. and M.H.). The latter relied upon the physiological signals routinely used in the R&K classification (2 EEG, 2 EOG, 1 EMG).

**Results**: Preliminary results obtained from 3 subjects show an automatic/visual agreement of 96.2% (inter-expert agreement of 96.6%) for the Sleep-Wake classification, and an agreement of 89.5% (inter-expert agreement of 94.1%) for the Wake-REM-NREM classification. A statistical epoch by epoch comparison on the 15 subjects will be presented.

**Conclusions**: These preliminary results suggest that the automatic software ASEEGA is accurate and will be a useful addition to the physician’s tools for ambulatory screening.


**P 171**

Night to Night Variability of Results of Ambulatory Pulse Oxymetry Monitoring

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**Objective**: The aim of this study was to evaluate the ‘night to night’ variability of ambulatory nocturnal monitoring of arterial blood oxygen saturation.

**Design and Methods**: We studied 20 ambulatory patients (pts) (mean age 43 ± 7, 17 male and 3 female) who were screened for the presence of sleep-disordered breathing (SDB). The nocturnal monitoring of arterial oxygen saturation (SAO2) was performed with pulseoxymeter ‘NONIN 8500M’ (USA). The recorded signal was the 4-s sampling frequency for digital storing in the oxymeter. All pts underwent two consecutive night continuous non-invasive monitoring of SaO2 under same conditions. The results obtained were analyzed with custom-made software ‘ARM-SaO2’. We evaluated the index of desaturation (ID-amount of incidence of 4% desaturations from the baseline stable value divided by monitoring time), minimum SaO2 (min SaO2), variability of SaO2 (Var SaO2-standard...
deviation of average value) and average value of SaO₂ during the monitoring. The presence of SDB was confirmed when the number of 4% desaturation was equal and more than 15 per hour, or presence of group episodes of 4% desaturation below 90%. Differences in estimated parameters between two nights were tested by Student t test.

Results: In 7 pts we revealed desaturation signs of SDB during the first night of monitoring and second night, too. The reproducibility of other variables are presented in table below (M ± STD).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>ID (h)</th>
<th>M SaO₂ (%)</th>
<th>Min SaO₂ (%)</th>
<th>Var SaO₂ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st night</td>
<td>7.1 ± 0.1</td>
<td>95.1 ± 2.7</td>
<td>80.5 ± 4.7</td>
<td>1.9 ± 1.4</td>
</tr>
<tr>
<td>2nd night</td>
<td>6.8 ± 0.8</td>
<td>95.5 ± 2.4</td>
<td>80.9 ± 4.6</td>
<td>1.9 ± 1.4</td>
</tr>
<tr>
<td>STD (Δ)</td>
<td>1.5</td>
<td>1.1</td>
<td>6.6</td>
<td>0.3</td>
</tr>
<tr>
<td>K variation</td>
<td>21.1</td>
<td>1.2</td>
<td>7.0</td>
<td>15.2</td>
</tr>
<tr>
<td>P</td>
<td>0.4</td>
<td>0.1</td>
<td>0.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Conclusion: the results from the first night of pulse oximetry do not differ significantly from those of the second night in ambulatory patients with suspected sleep-disordered breathing, provided that the method is appropriately standardized.

P 172
The SleepStrip compared to an 8-channels cardiopulmonary monitoring device in the screening of Sleep Disordered Breathing (SDB)
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Introduction: SDB is a common disorder affecting 2% of females and 4% of males in the adult population (1,2). SDB is associated with increased cardiovascular morbidity; studies have shown increased mortality of SDB patients mainly from cardiovascular causes (3). Moreover, SDB patients with excessive daytime sleepiness are at higher risk for motor and work-related accidents. However, it is estimated that the vast majority of these patients remain undiagnosed. Aim of our study was to assess the accuracy of the SleepStrip (SLP, Israel) device, a low cost disposable cardiorespiratory monitoring system the Polymesam (MAP, Germany) for the screening of patients with suspected SDB.

Methods: 33 consecutive adult patients (5 F and 28 M) referred to our Sleep Disorders Center for suspected SDB were included. All subjects underwent one night of simultaneous use of the SleepStrip (SS) and of the Polymesam (PM). Age ranged between 32 and 68, BMI between 22 and 34. Polymesam recordings were visually scored by two expert scorers who were blinded to the SS final score. Pearson correlation was computed between RDI (PM) and SS scores. RDI thresholds were defined as: 15-24: mild, 25-39: moderate and ≥40: severe SDB.

Results: one subject was removed from the analysis due to insufficient total sleep time. Correlation between the two scorers was r = 0.99 and between SS score and RDI was r = 0.85, p < 0.001 for both scorers. Measures of accuracy using the SS score thresholds (mild ≥1, moderate ≥2, severe ≥3) against RDI thresholds (mild ≥15, moderate ≥25, severe ≥40) were calculated. Sensitivity in the three thresholds categories was 0.93, 1.00 and 0.7; specificity 0.71, 0.64 and 1.00; positive predictive value 0.72, 0.56 and 1.00; negative predictive value 0.92, 1.00 and 0.93; overall accuracy 0.81, 0.75 and 0.94. Sensitivity values using the SS score threshold held constant at mild or above against three RDI thresholds (mild ≥15, moderate ≥25, severe ≥40) were respectively 0.93, 1.00 and 1.00.

Conclusion: Beyond the two blinded scorers and regardless of the cut-off method used, measures of accuracy were very high, particularly when the SS score threshold was held constant at mild and above.

We conclude that the SS in its current version seems to be a useful tool that enables physicians to confirm or reject the suspicion of SDB, as well as to determine the severity of the condition.

References:

P 173
Development of Sleep Forecast Method by Fluctuation Time Series Analysis Utilizing Finger Plethysmogram
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1Deltatooling Co., Ltd., 2Kanazawa University Graduate School of Medical Science, 3Shimane Institute of Health Science, 4Faculty of Engineering, Chiba Institute of Technology, 5School of Engineering, The University of Tokyo

Aims: This research aims at forecasting not sleepiness but subjects’ state just before their body begin to prepare for sleeping and transit to sleep state in real time.

Methods: The mutual effects of an oscillator and homeostasis, which govern sleeping and waking rhythms, are made apparent in changes in the heartbeat, breathing, and body temperature. Fluctuation occurs within the variation in the heartbeat, breathing, and body temperature,
and it was hypothesized that the progression from a waking state to a sleeping state could be observed by way of these fluctuations. In addition, a spectrum analysis done on changes in the heartbeat was divided into low frequency (LF), high frequency (HF), very low frequency (VLF), and ultra low frequency (ULF) areas, and it is said that activity regulating the body temperature is included in this VLF area. On one hand, the amplitude of the finger plethysmogram is governed by the heart’s fluctuation characteristics; so is affected by contraction and expansion, and by variations in blood pressure. Furthermore, fluctuations in the baseline are due to fluctuation in the blood flow, which in turn translates into variations in the diameters of the skin’s blood vessels. This led us to hypothesize that indicators of a subject entering a sleep state are captured in the gradient time series wave form of the square of the amplitude of the finger plethysmogram pressure, and also are captured in the fluctuation in diameters in the blood vessels in the skin as evidenced in the largest Lyapunov value’s gradient time series wave form, and that indicators of entering a sleep state exist in the VLF and ULF. The slide calculation method was used to find the gradient time series waveform, based on a 90% overlap rate with the time frame in which the gradient time series wave form was 180 degrees.

Results: This hypothesis was verified in sleep studies on subjects in both lying and sitting positions, and indicators were detected when the subject went from a waking state to the first stage of entering a sleep state. These indicators required a measurement timeframe of 30-50 minutes, and were captured when the power value’s gradient amplitude, the largest Lyapunov coefficient and the power value’s gradient exhibited a phase difference of 180 degrees.

Conclusion: The proposed method in this research made it a reality to forecast subjects’ state before transit to a sleep state in real time by capturing both amplitude and base line fluctuations of finger plethysmogram.

P 174

EEG Arousals < 7 Seconds in Duration Do Not Cause Any Change in Autonomic Nervous System Response Measured by Heart Rate Variability

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Aims: Current criteria for scoring electroencephalography (EEG) arousals use a minimum duration of at least three seconds. The minimum duration criteria was a methodological decision rather than physiological one. The aim of this study is to compare sleep stage 2 epochs with arousals of varying duration to stage 2 epochs without any arousals with regard to Heart Rate Variability (HRV) analysis to assess autonomic nervous system (ANS) responses to these events.

Subjects and Methods: 20 males (mean age: 51 ± 6; BMI: 29.5 ± 4.8 kg/m²; AHI: 18.8 ± 23.8; ODI: 17.1 ± 20.9; Arousal Index: 24.6 ± 15.6) underwent full polysomnography (PSG) in a sleep laboratory. Electrocardiography (ECG) and respiratory parameters including RIP belts, SpO₂, snoring and nasal pressure derived airflow were recorded. Standard methods were used to score sleep stages, arousals and sleep disordered breathing. Arousals were further classified based on duration into short (3–<7 seconds), medium (≥7–<11 seconds) and long (≥11–<15 seconds) arousals. HRV interbeat and frequency parameters were analyzed from the ECG and summarized in 5-minute epochs.

Results: Stage 2 epochs with short, medium and long arousals were compared separately to stage 2 epochs without any arousals with regard to HRV. The results are shown in the table below.

<table>
<thead>
<tr>
<th>RR intervals (ms)</th>
<th>Short Arousal (3–&lt;7 sec.)</th>
<th>No Arousal</th>
<th>t</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDNN</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VLF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LF</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>HF</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>TP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LF/HF</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Medium Arousal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RR intervals (ms)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDNN</td>
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<td></td>
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<tr>
<td>VLF</td>
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<td>LF</td>
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<tr>
<td>HF</td>
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<tr>
<td>TP</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>LF/HF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long Arousal</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

SDNN: Standard Deviation of all RR Intervals; VLF: Very Low Frequency; LF: Low Frequency; HF: High Frequency; TP: Total Power; LF/HF: Ratio of Low Frequency to High Frequency Components; sec.: seconds

Conclusions: Arousals that are less than seven seconds in duration do not have any effect on the ANS responses or the sympathovagal balance (LF/HF Ratio) measured by HRV. Greater shifts in sympathovagal balance are seen with increasing arousal duration. Arousal scoring criteria should...
take into account physiological responses to arousals rather than methodological considerations and inter-rater reliability when minimum duration criteria of arousals are considered.

**P 175**

Upper airway assessment of patients after uvulopalatal flap using computer aided measurements (CAM)

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Uvulopalatal flap (UPF) is a new surgical technique used to enlarge the upper airway, with the benefits of reversibility and higher patient tolerance. Computer aided measurements (CAM) has enabled us to objectively document improvement in upper airway dimensions. This is a prospective study involving ten patients who underwent UPF. Upper airway dimensions were made at retropalatal level pre and post operatively using CAM technique. Improvement of airway dimensions post UPF were compared with patient who underwent uvulopalatopharyngoplasty (UPPP). Our results show that patient who underwent UPF had similar percentage increase in upper airway dimensions as compared with patients who underwent UPPP.

**P 176**

Establishing of Sleep Stages in EEG, EMG AND EOG Signals using Neural Networks

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Sleep stages have different waveform which includes beta, alpha, theta and delta subbands. In this study, a complex method for classifying sleep stages was developed. Initially, the EEG signals obtained from 30 healthy different subjects under full-night polysomnography were separated to its subbands by using wavelet transform. Spectral components of these subbands were introduced as inputs to an artificial neural network (ANN). Similar procedures were applied on EMG and EOG signals by using same subjects. Experts in EEG, EMG and EOG interpretation inspected visually the data for the requirements of the ANN training. ANN gives five discrete outputs namely stage 1, stage 2, stage 3, stage 4 and REM sleep stage. The correct classification rate of the sleep stages were 90%. This result suggests that the automatic recognition algorithm can be helpfull for “sleep center team” to interpretation in recordings that take long time for the staging between the sleep stages.

**P 177**

Sleep-related breathing disorders occur with increasing frequency with rising severity of ventricular arrhythmia

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Greater prevalence of sleep-related respiratory disorders is known for certain diseases associated with higher-degree arrhythmia.

**Objective of the study:** To determine the prevalence of sleep-related breathing disorders among consecutively included, non-selected patients with ventricular arrhythmia.

**Method:** We performed a prospective study of 133 patients (78.2% male; mean age = 57). These patients underwent long-term ECG and, simultaneously, registration with a validated outpatient sleep-apnoea monitoring system (ApnoeScreen Pro®; JAEGER). We subsequently analyzed the correlation between the degree of severity of ventricular arrhythmia as determined by long-term ECG registration (LOWN classification), and any existing sleep-related breathing disorders.

**Results:** We determined an apnoea-hypopnoea index (AHI) of $\geq 10/h$ (mean $= 12.8 \pm 14.0$) among 36.8% of patents with high-degree ventricular arrhythmia (LOWN III and greater). In contrast, the prevalence of sleep-related breathing disorders was only 20% ($p = 0.038$) for the group with LOWN I-II ventricular arrhythmia, and only 16.3% ($p = 0.019$; LOWN 0 vs. LOWN I-II $p = 0.79$) for patients without ventricular arrhythmia. Overall, the prevalence of LOWN III or higher arrhythmia in the group with confirmed sleep-related breathing disorders was 45.16%. In contrast, the prevalence of high-grade arrhythmia among patients without sleep-related breathing disorders was only 23.53% ($p = 0.01$).

**Conclusions:** Among patients with high-grade ventricular arrhythmia there is significantly greater prevalence of sleep-related breathing disorders in comparison to patients with LOWN 0-II. We consequently believe that examination with respect to the possibility of discovering sleep-related breathing disorders requiring therapy should take place among patients diagnosed with high-grade arrhythmia.

**P 178**

Correlation Between Epworth Sleepiness Scale and Drowsy Driving.

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**Aims:** To determine the validity of Epworth Sleepiness Scale in predicting sleeping while driving. More than 100,
000 motor vehicle accidents annually are sleep-related. An estimated 70 million adult Americans have clinically significant sleep problems. The annual indirect cost estimate of sleep-related problems is $50-$100 billion, due to accidents, litigation, property destruction, hospitalization, and death. More efforts need to be done to increase public awareness of the magnitude of this public health burden.

**Methods:** We have retrospectively reviewed the charts of 50 patients (20 females, 30 males, aged 29-77 year-old) who were referred to the Cascade Valley Sleep Disorders Center for evaluation of a variety of sleep disorders. After obtaining a comprehensive sleep history, all patient underwent a thorough general and neurological examination, followed by an over-night in-lab Polysomnogram, some patients underwent a Multiple Sleep Latency Test as well.

**Results:** Our data showed that 30 patients (60%) scored over 9 in Epworth Sleepiness Scale, yet only 20 patients (40%) were complaining of being drowsy and/or falling asleep while driving. Of those 20 patients, 2 patients (10%) scored less than 9 in Epworth Sleepiness Scale. The mean age of those 20 patients was 49.05 year-old. Amongst them, 19 patients (95%) were diagnosed with Obstructive Sleep Apnea Syndrome, 6 patients (30%) with Psychophysio logic Insomnia, 3 patients (15%) with Restless Legs Syndrome, 3 patients (15%) with Idiopathic Hypersomnia, 2 patients (10%) with REM Behavior Disorder, 2 patients (10%) with Non-REM Parasomnia, and one patient (5%) with Narcolepsy.

**Conclusion:** Epworth Sleepiness Scale may not be always an accurate indication for drowsy driving. Clinicians need to specifically ask their patients about drowsiness while driving. Federal regulations, similar to those for medical disorders such as epilepsy, need to be developed and implemented. Such a step is necessary in order to make our roads safer and prevent further loss of lives.

**P 179**

Functional neuroanatomical correlates of spectral EEG power during NREM sleep

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**Aims:** The different stages of NREM sleep are defined by specific changes in brain oscillatory behaviour, resulting in surface EEG patterns like the sleep spindles, and delta or theta activity. Combining simultaneous EEG and fMRI acquisition allows to investigate the brain structures and network activities that are involved in generating and maintaining these oscillations in human subjects.

**Methods:** In the present study, the regional hemodynamic patterns linked to sleep-related oscillations were investigated in 15 subjects (7m, 8f; mean age 25.5 ± 4.5 years) during the first sleep cycles, starting from 23:00 hrs onwards after 36 hours of total sleep deprivation (1.5T GE, 20 slices EPI-BOLD, 33 min acquisition time, TR = 10s, TE = 60ms). After eliminating the artefacts induced by the switching gradients from the EEG, the spectral power of the delta, theta, alpha and the spindle frequency bands were computed using an in-house software and used as regressors for analysis in SPM2.

**Results:** Removing trials containing insufficient sleep or movement artefacts resulted in 15 trials (9 subjects) suitable for analysis. Alpha activity (8–12 Hz) correlated with activity in the thalamus and cingulate gyrius. Spindle activity (13–15 Hz) correlated with a more widespread pattern including frontal and parietal areas. Increases of slow oscillations (delta and theta frequency band) correlated with a decrease of hemodynamic response in the cingulate cortex, the thalamus and the insular cortex.

**Conclusions:** The results are in accordance with results of studies using PET and EEG analysis, and allow for a higher temporal and spatial accuracy of the dynamic patterns. The findings strengthen the influence of a resting brain activity and fast-paced, dynamic vigilance changes on fMRI activation maps.

**P 180**

Phase coordination ratio (PCR) and total Coordination of heart rate and respiration in healthy people

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**Introduction:** Measuring cardiorespiratory coordination (CRC) during sleep opens up interesting applications in sleep medicine. High CRC at night relates to Delta sleep and health. In our current study we present new methods, the so-called “Total Coordination” (ToC) of heartbeat and breathing and its “Phase Coordination Ratio” (PCR) i.e. the weighted average of the frequency ratio between heartbeat and breathing during the coordination of these functions.

**Methods:** In 35 healthy test persons (women: 14, men: 21) with a mean age of 45.3 years (SD: 16.7, range 25-84), heart action (EEG) during sleep was monitored via MK2 recorders and inspiration was measured with a thermistor. All participants completed a sleep protocol based on Hecht upon awakening. The classic parameters of heart rate variability (HRV; very low frequency-VLF, low frequency-LF, high frequency-HF), the PCR, the ToC (number of coordinated heartbeats) and the quotient of pulse and respiration (QPR) were monitored between 0.00hrs and 06.00hrs. The evaluation of the PCR, ToC and QPR in each case was carried out across an analysis window of 500 heartbeats which, with an adjustment of 100 heartbeats, was then adjusted across the whole period monitored.

Results: All HRV standard parameters except for the HF showed a significant relation to age (VLF: r = -0.47, LF r = -0.34, p < 0.05), but not the QPR, PCR and ToC. The average value of the PCR was 4.14 (SD = 0.74) and the ToC = 0.29 (SD = 0.10). Both parameters show a rhythmically structured progress with period lengths of 60–120 minutes.

Discussion: There is a strong connection between vagal activity of the autonomous nervous system and HF. However, in this study we saw no significant relation with age as the number of older participants was comparatively low. The PCR showed values across the group of around 4 which are, however, individually stable. It can therefore potentially be considered as a reliable but individual marker for the coordination of heartbeat and breathing. The ToC seems to reflect the basic rest-activity cycle (BRAC) and could therefore also deliver clues as to the sleep pattern. In future we will need to study whether these values show sufficient correlations with polysomnographic parameters.

Biological Rhythms

P 181
Does Handedness affect Sleeping Behavior?-An Actographic Study

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Aims: The aim of this study was to find out whether there are differences in sleep duration or rhythmicity between left- and right-handed subjects.

Methods: Sleep and activity patterns were continuously registered for 10 days using actometers on 20 left-handed and 20 right-handed students in Berlin. To determine their handedness a modified version of the Edinburgh handedness inventory was used. Each participant wore an actometer on each wrist. For evaluation of the data Actiwatch Sleep Analysis Software (CNT, UK) was used, statistical calculation was performed with a non-parametric variance analysis.

Results: We could show a significant difference in mean actual sleep time between left-handers (7.9h) and right-handers (7.3h) (p < .025 for measurement on the dominant and p < .013 for the non-dominant hand). By contrast evaluation of the FFT frequency analysis showed no difference between the two groups, with most subjects having a main frequency of a little less than 24 h.

Conclusions: While rhythmicity seems to be unaffected by handedness it seems to have an influence on sleep time. This might either be caused by the higher effort for left-handers to cope with our right-handed world or it might be due to structural brain differences.

P 182
Effects of age and rotating shifts on sleep of shift workers at a nuclear power plant

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Aims: To examine the effects of age and rotating shifts on sleep of shift workers at a nuclear power plant.

Methods: Data on the mean bedtime and wakeup time while working morning, afternoon and night shifts, as well as during leisure time, were gathered through face-to-face interviews with 257 shift workers working at a nuclear power plant (38.6 ± 8.7 yo; range 21–61 yo). They rotate a schedule of three shifts-morning (07:00–15:00 h), night (23:00–07:00 h) and evening (15:00–23:00 h)-and typically work 5 to 6 days followed by 3 to 4 days off.

Results: The mean (±SD) sleep length during leisure time and after morning, evening and night shifts was 8.3 ± 1.4 h, 6.6 ± 1.3 h; 7.4 ± 1.4 h and 5.5 ± 1.8 h, respectively (F (3, 705) = 104, p < 0.001). Older shift workers have a significant earlier wakeup time and shorter sleep length both during days off (r = -0.24 and r = -0.14, p < 0.05 for both) and while working evening shifts (r = -0.28 and r = -0.24, p < 0.05 for both). There were no significant correlations between age and sleep length during morning or nights shifts (r = 0.10 and r = 0.04, p > 0.05 for both). Furthermore, 52% of workers aged 45 year or older and 58% of younger people reported that they were satisfied or very satisfied with the quality of their sleep after night shifts (Z = 0.9, p > 0.05).

Conclusions: All shifts, and particularly the night shifts, resulted in shorter sleep length when compared to leisure time. If the sleep length during leisure time is considered as the expression of the physiological need for sleep, our results suggest that shift workers accumulate a sleep debt even when they work shifts with a late start, e.g., the evening shift. The significant, although weak, negative correlation between aging and sleep length during days off (r = 0.24, p < 0.05) possibly indicates the need for people to adjust to nigh shifts and experience an increase in sleep disruption.

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Physiology/Endocrinology

P 183
Relationship between endothelin-1 level and the severity of obstructive sleep apnea

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Aim: To examine whether circulating endothelin-1 levels correlate with the severity of disease in patients with obstructive sleep apnea.

Methods: Prospective nonrandomized study. Referral sleep laboratory for patients with sleep-disordered breathing and biochemistry laboratory. Patients Forty-two subjects (mean ± SD age, 51 ± 11 years) who were referred for suspected sleep apnea underwent an overnight sleep study and fasting morning venous blood sampling. Patients were divided into 3 groups with respect to apnea-hypopnea index: (1) severe sleep apnea (n = 12), apnea-hypopnea index greater than 20; (2) mild sleep apnea (n = 14), apnea-hypopnea index between 5 and 20; and (3) nonapneic control (n = 16), apnea-hypopnea index less than 5.

Results: Endothelin levels (mean ± SD) were 21.2 ± 8.6, 16.2 ± 5.2, and 10.6 ± 7.5 ng/L (P < 0.05) in patients with severe and mild obstructive sleep apnea and nonapneic controls, respectively. Plasma endothelin-1 levels correlated positively with the degree of sleep-disordered breathing as recorded by the apnea-hypopnea index (r = 0.59, P < .001) and percentage of sleep time spent with oxygen saturation below 90% (r = 0.35, P < 0.05).

Conclusions: Circulating endothelin-1 concentrations in patients with obstructive sleep apnea, independent of body mass index and age, are significantly higher than levels in nonapneic controls and there is a positive relationship between endothelin-1 concentrations and the severity of sleep apnea. High level of endothelin-1 may be a prognostic marker of obstructive sleep apnea syndrome.

P 184
Relationship between Cycling alternating pattern (CAP) expression and Growth Hormone (GH) deficiency in young adults with Prader-Willi Syndrome and GH deficiency of childhood onset

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Introduction: The relation between growth hormone deficiency (GHD) and sleep is poorly understood and the effect of GH replacement therapy on the sleep electroencephalogram is controversial. Moreover no report exists about the analysis of arousals and Cycling Alternating Pattern (CAP) in GH deficient patients. Objective: we studied the relationship between GHD and sleep variables including arousals and CAP, in two groups of adult patients with GHD.

Patients and Methods: one group included 11 males and 7 females (mean age: 27.5 ± 5.5 years) with Prader-Willi Syndrome (PWS), a complex genetic disorder involving the hypothalamus-pituitary axis, characterized by GHD, hypogonadism, mental retardation, obesity, increased risk for sleep apneas and hypersomnia. PWS patients were evaluated at baseline and after 6 months of recombinant human GH therapy (rhGH). The second group included 5 males and 4 females (mean age 25.5 ± 7.4 years) with idiopathic GHD of childhood onset (COGHD) taking rhGH therapy from at least 6 months. Patients were submitted to a full-night complete polysomnography and the Multiple Sleep Latency Test (MSLT). GHD was evaluated by standard GH peak response after GH-releasing hormone plus arginine test. 15 normal subjects, 7 males and 8 females (mean age 28.2 ± 7.2) were recruited as control group.

Results: compared to controls PWS group presented reduced MSLT score (7.2 ± 2.9 min. vs 15.3 ± 7.2 min.; p < 0.001) confirming hypersomnia, and increased number of REM periods (7.8 ± 3.8 vs 4.1 ± 2.4). Sleep efficiency was similar in the two groups. Severe obesity was present in PWS group (mean BMI = 47.9 ± 8.6), but only four patients had Apnea/Hypopnea Index (AHI) ≥ 5. In the subgroup of 14 PWS patients with AHI < 5 CAP rate (percentage of total CAP time referred to total NREM sleep) was increased compared to controls (26.5% ± 8.3 vs 21.5% ± 4.3; p = 0.038), independently from age, arousals, respiratory disturbance variables or BMI. GH peak response negatively correlated with CAP rate (r = -0.47; P = 0.045) but not with other sleep parameters, BMI or severity of illness variables. Moreover 6 patients with CAP expression characterized by a proportion of A1 subtypes ≥ 60% referred to total A Phases presented less severe GHD compared to 8 patients with A1 subtypes proportion < 60% (GH peak response = 9.7 ± 3.8 ng/ml vs 4.5 ± 2.2 ng/ml; p = 0.01), independently from age. After six months of rhGH therapy CAP rate resulted significantly reduced (22.3% ± 5.2) compared to baseline and 11/14 PWS patients presented a proportion of A1 subtypes ≥ 60%. Respiratory disturbance variables, MSLT score were not affected. In COGHD group sleep parameters, CAP rate, proportion of phase A subtypes of CAP and MSLT score were comparable to control group.

Conclusion: our preliminary study suggests an hypothalamic involvement in CAP expression in GHD patients, with the possible mediated of GH and independently from age.
Baroreflex Sensitivity and Ventricular Premature Beats during Sleep in Coronary Artery Disease Patients

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Aim of the study was to investigate the modifications of baroreflex sensitivity (BRS) during episodes of ventricular premature beats (VPBs) and paroxysmal supraventricular tachycardia (SVT) during sleep in coronary artery disease patients (CAD pts).

Methods: Polysomnography was performed in 82 CAD pts. Patients were divided in two groups: 1) 43 patients with more than one VPB per sleep hour (mean age 58 (SD 6.8) yrs., 33 men and 10 women), and 2) group, 39 patients without VPBs (mean age 61 (SD 10.0) yrs., 28 men and 11 women). The groups were matched according body mass index and leading pathology: arterial hypertension, diabetes mellitus, angina pectoris and congestive heart failure. Episodes of paroxysmal SVT (6-14 beats) were observed in 17 CAD pts (mean age 59 (SD 9.7) yrs., 14 men and 3 women). Finger blood pressure and heart rate during sleep were monitored beat-by-beat non-invasively, using “Porta-press” (model-2) device. BRS was assessed as the slope of the regression line between spontaneous increases or decreases in systolic blood pressure and the related lengthening or shortening in the RR interval, occurring over spontaneous sequences of three or more consecutive heart beats. The mean value of BRS was calculated in different sleep stages containing frequent VPBs and sleep stages free from VPBs as well as during every four minutes before and after episodes of paroxysmal SVT.

Results: CAD pts with VPBs, as compared with pts without VPBs, demonstrated lower values of BRS during wakefulness (8.4 ± 4.4 and 9.3 ± 4.0 msec/mmHg, respectively). In both groups BRS gradually decreased from wakefulness till stage 4 (8.2 ± 6.5 and 8.4 ± 3.4 msec/mmHg, respectively in pts with and without VPBs) and reached nadir values in REM sleep (7.0 ± 4.0 and 8.0 ± 2.9 msec/mmHg, respectively). The lowest values of BRS were found during REM sleep in CAD pts with VPBs. The modifications of arterial systolic blood pressure during different sleep stages in both groups did not differ significantly (p > 0.05). Four minutes before the onset of paroxysmal SVT BRS started to decrease reaching the nadir (6.5 ± 2.9 msec/mmHg) just before the paroxysmal tachycardia. After the spontaneous conversion of paroxysmal SVT into the sinus rhythm BRS started to increase (6.8 ± 2.9 msec/mmHg), however did not reach the baseline level before the paroxysmal SVT (7.6 ± 3.3 msec/mmHg, p < 0.05). No significant differences of arterial blood pressure and heart rate frequency before and after the episodes of paroxysmal SVT were found.

Conclusions: CAD patients with PBs, as compared with patients without PBs, demonstrated lower baseline level of BRS at wakefulness and reduced BRS modifications over individual sleep stages displaying the nadir values during REM sleep. A gradual decrease of BRS just before the paroxysmal SVT was observed. Decreased BRS, especially during REM sleep, reflecting reduced autonomic heart rate control, might be provocative factor for cardiac arrhythmias.

Molecular Biology/Immunology

No Influence of beta2 Adrenergic Receptor Polymorphisms on the Severity of Cardiovascular Risk Factors in Patients with Obstructive Sleep Apnea

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Background: The increased sympathetic nervous activity in obstructive sleep apnea (OSA) patients is mainly responsible for the high prevalence of arterial hypertension, and is suggested to deteriorate triglyceride and high density lipoprotein cholesterol levels in these patients. The functional relevant polymorphisms of the beta 2 adrenergic receptor (T-47C/A16G and G27C) have inconsistently shown modifying effects on these risk factors in previous studies.

Methods: In this group we tested the ADRB2 polymorphisms and the 5 most frequent haplotypes for their modifying effects on the OSA-induced changes of blood pressure (BP), heart rate (HR) and lipid levels. We further compared the prevalence of cardiovascular risk factors, coronary heart disease (CHD, n=55,12.8%) and survived myocardial infarction (MI, n=27, 6.3%) between the genotypes (GT) and haplotypes (HPT).

Results: Multivariate linear/ logistic regressions revealed a significant and independent (covariates: body mass index, age, gender) influence of the severity of OSA on daytime systolic, diastolic BP, HR, prevalence of hypertension, triglyceride and HDL levels (all p<0.01). The ADRB2 genotypes and haplotypes did not show any modifying effects on these relations, as well as on the prevalence of dyslipidemia, diabetes and CHD. However the heterozygous variants of all three polymorphisms had a significant
lower relative risk for survived MI (T-47C: n = 195, odds ratio (OR) = 0.32, p = 0.012; Arg16Gly: n = 197, OR = 0.39, p = 0.031; Gln27Glu: OR = 0.37, p = 0.023). Carriers of the most frequent haplotype (n = 113) with heterozygosity in all three polymorphisms showed a five fold lower prevalence of survived MI: OR = 0.21, p = 0.023.

Conclusions: Our study showed no significant modifying effect of the functional relevant ADRB2 polymorphisms on OSA conducted BP, HR or lipid changes. However, in our group with on average high cardiovascular risk profile, heterozygosity of these polymorphisms is associated with a lower prevalence of survived MI.

P 187
Association of genetic markers with obstructive sleep apnoea

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OSA is a complex disease process, its aetiology is multifactorial and incompletely understood. OSA is a common disease and a major public health problem. Familiar aggregates have been documented in several reports of OSA syndrome, and several candidate genes have been identified.

The aims and Objectives: To study the genetic association of patients with severe obstructive sleep apnoea

To analyse the genetic parameters involved in obstructive sleep apnoea

Methodology: This is a prospective study comparing the presence of the candidate genetic markers between 15 patients with OSA proven on polysomnogram and 15 controls. Extracted DNA was analysed for the following markers such as Tumour Necrosis Factor (TNF-alpha), Fibrillin, and Connective Tissue Growth Factor (CTFG).

Results and Conclusion: In our limited study, thirty specimens were subjected for PCR with TNF-alpha, fibrillin and connective tissue growth factor (CTFG). Two specimens in the OSA group were positive for TNF-alpha and one specimen was positive for fibrillin, whereas all the genetic markers in the control group were negative. The presence of the Fibrillin gene is also associated with craniofacial dysmorphism and tissue laxity in the upper airway, and the presence of TNF-alpha is associated with obesity. The presence of these two genes suggests that there may be a genetic component in OSA.

Pharmacology

P 188
Beware of depressive stroke patients with sleep complaints

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Depression after stroke is a common phenomenon. Since tricyclic antidepressants may have harmful side effects, mirtazapine is increasingly used as an effective psycho-pharmacological treatment of depressive disorders especially in patients with sleep complaints. On the other hand, more than two thirds of stroke patients suffer from sleep apnea. A recent study (Castillo et al. 2004) showed an 80% reduction of the respiratory disturbance index (RDI) by mirtazapine. Because of these promising results, we tried mirtazapine in six stroke patients who suffered from severe sleep apnea and refused a CPAP device. Standard polysomnography was between 2200 and 0600 hours. The patients (all male, 67.7 ± 1.4 yrs (mean ± std.err.), BMI 27, 2 ± 1.4 kg/m², basal ganglia bleeding (n = 2), MCA ischemia (n = 3), basal ganglia ischemia (n = 1)) had a baseline RDI of 44.9 ± 4.9/h. Three of the patients had an effective CPAP treatment night (RDI 6.5 ± 1.8/h), but only one patient remained on CPAP. The patients (n = 3) who refused CPAP from the beginning, received mirtazapine as well as those before (n = 1) or after (n = 2) CPAP. One patient was lost for follow up after nine days of mirtazapine intake. Another patient had to stop mirtazapine after two weeks due to side effects, and he was convinced to begin with CPAP treatment. The remaining four patients had moderate increase in RDI (130.3 ± 13.3% of baseline) shortly after beginning of mirtazapine (intake duration 14.8 ± 4.7 d). After 52 ± 13.4 days the RDI was either reduced (57.1%, n = 2) or increased (164.2%, n = 2), thus mirtazapine was stopped in the latter two. However, none of the patients on mirtazapine reached an RDI below 30/h within the follow up time of maximum 79 days. Mirtazapine was effective in sleep consolidation in all patients, i.e. the sleep efficiency increased from 68.6 ± 6.5% to 78.5 ± 10.4%. The main conclusion of this small series on stroke patients is, that patients who receive mirtazapine, either to control post-stroke depression with sleep disturbances or to alleviate sleep apnea, should be examined for changes of breathing parameters during sleep. Mirtazapine may be effective in reducing the RDI thus dropping the risk for another cardiovascular event including new stroke. But mirtazapine may also worsen sleep apnea thus possibly secondarily aggravating the neurological deficits and/or hinder the recovery. Since mirtazapine, at the moment, is the only non-tricyclic sedating antidepressant, this may hamper the further use of that drug, at least in stroke patients. There also seem to be a time effect, since all patients slightly worsened in the beginning. The improvement may start only after 6 to 8 weeks. This implicates that the beneficial effect of mirtazapine is not simply due to its action on receptor systems but seems to originate in changes in proteins, genes or even structural modifications e.g. formation of new synaptic contacts. We therefore plan a study with a larger number of stroke patients and longer follow up time.
P 189
Effect of zopiclone on GABA(B) receptor expression and function in the dorsal horn of the rat spinal cord

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Aims: The present study was undertaken to examine whether the administration of zopiclone alters GABA(B) receptor subunit expression and function in the dorsal horn of the rat spinal cord.

Methods: For the study, rats were injected (i.p.) once daily with zopiclone for 7 consecutive days, during which their thermal withdrawal threshold was monitored, and after which GABA(B) receptor function, and the levels of GABA(B) receptor subunit mRNA, were quantified in the spinal cord dorsal horn.

Results: The results indicate that 5–7 days of continuous administration of zopiclone are necessary to observe a significant increase in the thermal pain threshold. Moreover, it was found that 7 days of treatment with zopiclone enhances GABA(B) receptor function, as measured by baclofen-stimulated [35S]GTPgammaS binding, and increases mRNA expression for the GABA(B1a) and GABA(B2), but not GABA(B1b), subunits.

Conclusions: Our findings suggest the effect of zopiclone is accompanied by a change in spinal cord GABA(B) receptor sensitivity that could be an important component in the response to this agent. This, together with results from other types of studies, indicates the potential therapeutic value of developing drugs capable of selectively activating, inhibiting, or modulating GABA(B) receptor function.

P 190
REM Sleep: Supression by a Monoamine Oxidase Inhibitor vs Rebound after CPAP Initiation

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Introduction: In 1971 Wyatt et al reported that monoamine oxidase inhibitors (MAOIs) “totally” suppressed REM sleep. However other conditions such as narcolepsy, sleep deprivation and nasal continuous positive airway pressure (nCPAP) are known to also modulate REM sleep. Patients with severe sleep apnea have been reported to have REM rebound after experiencing severe sleep fragmentation during the recovery phase with nCPAP that lasts approximately a week. There are limited opportunities to compare relative influence of these different factors on REM pressure. There are no published reports of whether REM rebound occurs for patients on MAOi therapy.

Methods/Results: The case of a 58 year old woman on chronic high dose tranylcypromine 90 mg a day divided dose (typical dose 30-60 mg a day) is presented. The medication was continued without interruption while she underwent polysomnography. She underwent a split night sleep study where she was found to have mild obstructive sleep apnea (OSA) with an apnea/hypopnea index of 13 events/hour. Her arousal index was 40/hour with 27% attributed to breathing (11/hour). During the first part of the study she did not have any REM sleep. Her mild OSA was treated with nCPAP. When titrated to 9 cm of water pressure during the second part of the study, she had 62 minutes of REM sleep (26% of the total sleep time).

Conclusion: REM rebound can occur even for relatively mild OSA even for a patient on chronic high dose MAOi therapy. This single case illustrates that the REM pressure that develops after initiation of nCPAP, even for milder OSA, is stronger than the effects of a MAOi, the gold standard REM suppressant medication.

P 191
Preliminary data on the Venlafaxine antinociceptive effects in cutaneous and visceral pain models

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Aim: Experimental research on venlafaxine potent antinociceptive effects in cutaneous and visceral pain models.

Material and Method: The experiment was carried out with white mice (20–25 g), divided into 5 groups of 7 animals each, treated orally with the same volume of solution for 10 days, as follows: Group I (DW): distilled water 0,3 ml; Group II (VLX-10): venlafaxine 10mg/kbw; Group III (VLX-20): venlafaxine 20 mg/kbw; Group IV (VLX + NLX): venlafaxine 20 mg/kbw. In the day of the experiment the following groups receives: Group IV (VLX + NLX): venlafaxine 20 mg/kbw orally + naloxone 5 mg/kbw i.p., Group V (IMC): indomethacin 30 mg/kbw i.p. Hot plate test was used to assess venlafaxine-induced antinociception. The model of visceral pain consists of cyclophosphamide-induced cystitis a recently-developed behavioural model of inflammatory visceral nociception. Data were statistically analyzed by Fisher-Tackey tests.

Results and Conclusions: Oral administration of venlafaxine (20 mg/kbw) resulted in a significant antinociceptive effect in hot-plate (p<0.05), manifested 15 minutes after the application of thermal stimulus. Venlafaxine (20 mg/kbw) also exhibited antinociceptive effect in cyclophosphamide-induced cystitis, but it’s effect is less potent then those of indomethacin (30 mg/kbw). The antinociceptive effect of venlafaxine was sensitive to blockade by naloxon
Children

P 192
Who comes to the Sleeplaboratory for Children?

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Introduction: Sleep disorders in children are common, but it is not clear which diagnoses prevail. Due to our work in a sleepcenter with special interest in sleep in children we are able to give insight in what kind of disorders are most common and can give some ideas on the prevalence of the various sleepdisorders in this population.

Methods: We searched our database for details of all children seen in the sleeplaboratory in the period from 2000–2004. The initial clinical diagnosis and the diagnosis after thorough work-up including structured history, polysomnography and often long-term actigraphy were compared and used for our analysis. The therapy that was chosen was taken into account as well.

Results: In the period of study 228 children were seen in our sleeplaboratory (130 M). Age range 0-18 yrs and median age 10 yrs. The main presenting diagnoses were various: insomnia (64%), parasomnia (9%), DSPS (8%), sleepiness during daytime (6%), OSAS (3.5%), chronic tiredness syndrome (2%), epilepsy (2%), narcolepsy (1.3%). After the work-up the diagnoses had changed for many of the patients. The main final diagnoses were: insomnia (17.5%), no sleep disorder (17%), limit setting disorder (15%), DSPS (15%), parasomnia (8%), sleep state misperception (6%). The diagnoses resulted in therapies tailored to the needs of the patients (and parents). The therapies for the main diagnostic groups were advices for the parents in the group of young patients (for example for limit setting disorders) and light and behavioral therapy for the DSPS patients.

Conclusion: The patients who came to the sleeplaboratory had initial diagnoses conform our expectations. After the work-up the diagnoses had to be changed in many instances with implications for the therapy, making the often laborious work-up worthwhile.

Sleep Deprivation

P 193
Chronic Sleep Deprivation: a Series

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Aims: To report our experience with 16 consecutive patients diagnosed with chronic sleep deprivation (SD) at our center over a period of 2 years.

Patients and Methods: Assessment of the 16 patients included a complete clinical history and neurological examination, a standard sleep-wake questionnaire, a conventional polysomnography (PSG), one (or more) multiple sleep latency test (MSLT), and a 2-week actigraphy. The diagnosis of chronic sleep insufficiency was made based on the following criteria: (1) subjective EDS (Epworth Sleepiness Scale $\geq$ESS $\geq$10), (2) PSG without sleep-disordered breathing (apnea hypopnea index <10) or periodic limb movements in sleep (PLMS-Index <10), (3) absence of other neurological, psychiatric or medical cause of EDS (including the use or abuse of medications/drugs), (4) history or actigraphic findings suggesting chronic sleep insufficiency.

Results: There were 2 (12.5%) women and 14 (87.5%) men with a mean age of 39.4±10.2 years (range: 23-56). The main reasons for referring these patients to our sleep clinic included EDS (53%), absence-like episodes (33%), impairment of concentration and/or cognitive performance (7%) and others (day-dreaming, fatigue, jerks, 7%). The mean ESS was 15±3 (range: 10–21). Subjectively, the estimated sleep duration (SQ) was 380±54 minutes on working days, and 502±148 minutes on weekends/holidays, respectively. Actigraphically, the time of rest/sleep was 355±55 minutes on working days and 412±82 minutes on weekends/holidays, respectively. On polysomnography a short sleep latency (mean 7.4±4.5 minutes to NREM2), a high sleep efficiency (mean 94±5%) and increased amounts of slow wave sleep (NREM stage 4, mean 17±5%) were found. On MSLT the mean sleep latency to NREM 1 sleep was 5.0±3.1 minutes. Three patients had one sleep onset REM period (SOREM), and one patient three SOREM. The HLA-DQB1*0602 haplotype was positive in 50% of the patients tested.

Conclusions: These data suggest a variable clinical presentation and conversely relatively stereotyped laboratory findings of chronic sleep deprivation. Sleep questionnaire, polysomnography ad actigraphy are essential for diagnosing this condition.

P 194
A Randomized, Double-blind, Placebo- and Active-Controlled Evaluation of Single Doses of Armodafinil in Healthy Subjects During a Period of Acute Sleep Loss

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Aim: Earlier studies with modafinil have shown a morning dose of 200 or 400 mg wears off later in the day, creating the need for supplemental therapy or BID dosing. A longer acting agent is needed in some patients to sustain attention and wakefulness with QD dosing. This study was designed to evaluate the effects of single 100- to 300-mg doses of armodafinil, the R-enantiomer of modafinil with a longer half-life, on wakefulness and ability to sustain attention in healthy subjects during a period of acute sleep loss.

Methods: One hundred and seven healthy male volunteers (aged 18 to 40 years) participated in this randomized, double-blind, active- and placebo-controlled study. Subjects underwent 28 hours of acute sleep loss (from 0700 on day 1 to 1100 on day 2) at a sleep clinic. A single dose of study drug (armodafinil 100 mg, 150 mg, 200 mg, or 300 mg; modafinil 200 mg; or placebo) was administered at 1925 on day 1 after a standardized meal. Wakefulness was assessed using the Maintenance of Wakefulness Test (MWT), which was performed at 2-hour intervals from 2200 on day 1 to 0800 on day 2. The ability to sustain attention was assessed using the Psychomotor Vigilance Task (PVT), which was performed at 2-hour intervals from 2110 on day 1 to 0910 on day 2. Blood samples for pharmacokinetic assessments were collected immediately prior to and after study drug administration and hourly for the next 14 hours. Adverse events were evaluated throughout the 2-day clinic stay and during a telephone interview conducted on day 9.

Results: All doses of armodafinil significantly improved wakefulness (MWT sleep latency) relative to placebo at 0100, 0310, 0510, 0710, and 0910 (p < 0.05). All doses of armodafinil also improved the ability to maintain attention (PVT median reaction time and number of lapses) relative to placebo at 0100, 0310, 0510, 0710, and 0910. On a mg/mg basis (armodafinil 200 mg vs modafinil 200 mg), armodafinil resulted in a higher plasma concentration that lasted longer post dose than modafinil and provided better sustained attention and wakefulness longer post dose. At doses that produced equivalent systemic exposure (armodafinil 150 mg and modafinil 200 mg), the mean peak armodafinil concentration was lower and higher concentrations were sustained for a longer period of time post dose. The most common treatment-related adverse events with armodafinil were abdominal pain and nausea.

Conclusions: Single 100- to 300-mg doses of armodafinil significantly improved wakefulness and the ability to sustain attention relative to placebo in healthy male volunteers with acute sleep loss. On a mg/mg basis armodafinil produced better and longer-lasting wakefulness and sustained attention than modafinil.

P 195
Opioids and Sleep

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Behavioral effects of opioid agonists’ action in humans and animals are complex because of coexisting excitatory and inhibitory behavioral patterns. Systemic administration of morphine in animals suppresses both slow wave sleep (SWS) and paradoxical sleep (PS) (1,2). The drug-induced insomnia is characterized by a prominent dissociation of waking EEG and behavioral parameters: EEG demonstrates the presence of high-voltage low-frequency waves, while behaviorally the animals remain awake and exhibit stupor (3, 4) or even active behavior. These observations emphasize the importance of determining the brain sites through which opioids alter EEG and behavioral arousal.

The aim of our study was to investigate the effects of opioid agonists on the organization of Sleep-waking behavior (SWB) in animals.

Experiments were performed in chronic preparations of adult cats (n = 4). To study the effects of opioids on the brain integrative activity we used Morphine, Tramadol and Nalbuphin (i.p. administration).

Our studies show that Opioid agonists caused alterations in both sleep and waking behavior, such as development of hallucinations (an unusual waking behavior such as “playing” with imaginary items, indifference to external sound and visual stimuli, non-typical EEG pattern of waking with intense PGO-spikes), and dissociation of EEG and behavioral parameters. Opioids induced total elimination of SWS and PS (TSD) for 5–24 hours. Subsequently, a rebound of deep SWS and an increase of PS amount occurred after the TSD period. This was followed by a gradual normalization of the SWB. Complete recovery of SWB developed in about 24 hr after the TSD period. Regular waking recovered first and only then sleep, with normal alterations of all its phases and stages.

These findings suggest that the opioid-induced TSD and modulation of the nervous system excitability should involve the central and peripheral opioid and/or non-opioid mechanisms of their action.

References

P 196
Gender effect on vigilance during sleep restriction
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Aims: This study evaluates the influence of gender on sleepiness and the ability to stay awake during 3 days of sleep restricted to 4 hours sleep per night.

Methods: 10 women and 8 men, aged 20–30 years, healthy and non-smoker were included in the study after a careful selection. The subjects were admitted to the sleep laboratory for one baseline night (11pm–7am), three nights of restriction (01–05am) and one recovery night (11pm–7am). Continuous EEG recordings were performed during days and nights.

The Stanford Sleepiness Scale (SSS) was performed every 2 hours to evaluate subjective sleepiness. The resistance to fall asleep was objectively assessed with the Maintenance of Wakefulness Test (MWT) performed twice daily at 8.30 am and 1.30 pm. Psychomotor Vigilance Test (PVT) was performed at 9 am, 1 pm and 5 pm.

Results: MWT: During the restriction, involuntary lapses appeared significantly more often among women than among men. The women frequently felt asleep in the morning at 8 am whereas the men showed a peak of sleepiness at 1 pm (Condition Effect: p = .000; Condition × Gender: p = .023).

PVT: During restriction, the number of lapses was significantly increased among women during the 3 sessions (9 am, 1 pm and 5 pm), while among men the number of lapses was only increased at 1 pm. The sessions at 9 am and 5 pm did not show any difference with the baseline (Condition: p = .003; Condition × Gender: p = .036; Condition × Gender × Hours: p = .059).

Stanford: The women felt particularly tired during the sleep restriction in the morning at 8 am; this effect decreased at 1 pm and did not exist any more at 5 pm. On the other hand, the men had an effect of restriction during the 3 sessions with a peak of sleepiness at 1 pm (Condition: p = .000; Condition × Gender × Hours: p = .028).

Conclusion: As a whole, the three tests suggest a greater vulnerability of the women to the effects of sleep restriction, mainly for objective measurements. In addition, the women were particularly affected by sleep restriction in the early morning (8–9 am), while the men showed a greater sleepiness at 1 pm, after the lunch.

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Behavior and Dreaming

P 197
Dream Recall In The Elderly After Spontaneous Awakenings In Laboratory

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Aims: Previous research showed that the frequency of dream recall in the elderly is lower than in the young. However, many of these studies were based on home diaries, not always filled immediately at awakening; thus, dream recall may be hampered by waking interference. Otherwise, dreams were recorded in the sleep lab after provoked awakenings, altering the natural sleep pattern. This study is aimed to assess the frequency and the length of dream recall in elderly subjects after spontaneous awakenings in the lab. A content analysis was also carried to detect the main qualitative characteristics of elders' dreams.

Method: Eight healthy elderly women (age range 65–78) participated in the study. Subjects slept two nights in the sleep lab (one for adaptation, one experimental). Immediately after each spontaneous awakening, detected through polysomnography and videorecording, they were asked to recall their mental activity through a conventional question. After this primary report, a guided report was obtained by asking questions concerning specific dream features, such as the environment and the presence of specific characters, with a procedure described in a previous paper. Reports were tape-recorded, written down and subposed to T.U. and content analysis.

Results: From a total number of 44 awakenings (13 from REM, 31 from NREM), 11 dream reports were obtained (25%). The frequency of dream recall was significantly higher in REM sleep than in NREM sleep (53.8% vs. 12.9%, p < 0.001). Mean length of the recall was 5.9 ± 5.1 T.U., and were longer in REM than in NREM reports. Guided reports were significantly longer than primary reports (17.2 ± 12.5 U.T. vs. 5.9 ± 5.1 U.T., p = 0.003). Dream recalls had a low score of “continuity” and a high score of “plausibility”, with no significant difference between REM sleep and NREM sleep awakenings (respectively 0.83 ± 0.3 vs. 0.48 ± 0.5 and 0.78 ± 0.2 vs. 0.71 ± 0.2).

Conclusions: Also in the sleep lab, the frequency of elders' dream recall is very low in the elderly, both after REM sleep and NREM sleep awakenings. This results suggests that the reduction with age of dream recall is not dependent on waking interferences. However, T.U. value of primary reports, similar to the one reported in young subjects, and the remarkable length of guided reports suggest that the process of dream production in the old individual is globally preserved. Consistently with anecdotal reports, elders' dreams seem more plausible, that is more similar to waking events, than young subjects.

P 198
Declarative memory performance after a one hour midday nap

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Aims: In the current literature it is heavily discussed in which ways sleep might be beneficial for memory consolidation. Former studies showed that sleep after learning is required for better performance on the following day. As far as naps are concerned, only few studies have been published until recently.

Methods: To find out whether naps have a positive effect on declarative memory consolidation, we tested 22 subjects aged between 19 and 30 years. They had to perform a declarative learning task (learning word-pairs prior to sleep) and were tested (cued recall) before and after one hour of napping.

Results: Overall performance was significantly greater after sleep than before the nap. The data indicates that only participants entering slow wave sleep during the midday nap could improve their memory performance. Different sleepiness could not account for this relationship. Furthermore, subjects that improved their memory performance showed more theta-power over all sleepstages of the midday nap than those who didn’t.

Conclusions: The study thus provides preliminary evidence that a 60-minutes nap including SWS at noon has a positive effect on declarative memory consolidation.

P 199
Trait of Derealization in Lucid Dreamers

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Aims: Lucid dreaming, first introduced by Frederik van Eeden (1913), is a dreaming state in which the dreamer is aware of the fact that he or she is dreaming. In spite of emphasized lucidity while dreaming, there arises a question as to whether lucid dreamers can be more lucid while awake than the others. In the present study, we investigated the relation between the trait of derealization and lucid dreaming in nonclinical sample.

Methods: Participants included 186 undergraduates (91 men and 95 women). They were administered the Derealization Questionnaire (Nasu, 1996) and Japanese version of Dissociative Experiences Scale-II (DES-II) (Bernstein & Putnam, 1986). The participants were also asked about the frequencies of dream parameters including lucid dreaming, false awakenings, out of body experiences, and sleep paralysis.

Results: In the present study, 13.4% of participants were lucid dreamers who experienced lucid dreaming more than once per week. There were significant correlations between the frequency of lucid dreaming and derealization score (Spearman’s rho = .229, p < .01), and between the frequency of false awakenings and derealization score (rho = .260, p < .01). Participants who experienced lucid dreaming once a week or more scored higher on the Derealization Questionnaire as compared with non-lucid dreamers (n = 161) (Z = 3.51, p = .000). Frequency of lucid dreaming was also correlated with DES-II total score (rho = .189, p < .01), and lucid dreamers scored high on DES-II (Z = 3.78; p = .000).

Conclusions: The present study showed that lucid dreamers scored high on the derealization scale and DES-II, indicating that they are prone to derealization or dissociated state while awake. Psychopathological aspect of lucid dreaming was pronounced by Stepansky et al. (1998), who stated that lucid dreamers more frequently reported family problems or nightmares. The phenomenon “lucid dreaming” might be related to psychopathology, and cautious practice of lucid dreaming should be recommended.

P 200
Dream recall an dream content in Posterior cerebral artery (PCA) stroke patients

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Modern dream theories attribute to the medial occipito-temporal (OT) region a role in the maintenance of the visual imagetic component of dreams. Sporadic case reports have led, however, to conflicting results, since some patients complain of having lost the ability to dream. In this study dream recall and content of unilateral medial OT lesioned patients (PCA stroke) were studied.

Hypothesis: Dream content of PCA stroke patients is impaired only in the visual imagetic component; Low dream recall is correlated to awake memory deficits.

Population: 12 unilateral PCA patients (7 right, 5 left); 12 controls without focal brain lesion.

Methods: Forced awakenings in PSG recording nights; 14 days dream diary; Dream content analysis by the Hall and Van de Castle coding system; Neuropsychological assessment-verbal memory, visual memory and spacial span (Weschler memory scale), language, Benton facial
Objective: The Watch-PAT100 is an ambulatory device based on the Peripheral Arterial Tonometry (PAT). It was validated against polysomnography and in a previous laboratory study we have evaluated the clinical guidelines for its clinical use.

Introduction: To evaluate the savings in full PSG studies in evaluating patients with suspected sleep apnea patients by using the Watch-PAT100.

Methods: Watch-PAT100 recordings were performed in 260 patients (male:female ratio 1:2.6, mean age 51 years

Results: There was a trend toward lower dream recall in PCA stroke patients, although only NREM recall in left PCA patients was significantly lower than controls. Dream recall was correlated with verbal memory. Patient dreams had significantly less expressive activity and distorted settings. Right lesions impaired visual activity, visual descriptions per dream and known characters recall. In these patients there was also impaired awake visual imagery and dream recall correlated with the recognition of unfamiliar faces.

Conclusion: This study supports the hypothesis that TO regions are essential for the visual imagery of dreams, especially the right TO lesion. Facial emotions recognition and bizarre settings may be specially impaired by the presence of either unilateral OT lesion. Lower dream recall might be related to verbal memory deficits.

P 201
On the necessity of studying differential effects of sleep on episodic vs. semantic memory

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Various EEG parameters observed during sleep (like delta waves and sleep spindle activity) have been associated with memory performance in recent years (Anderer et al., 2002, Nader & Smith, 2003, Schabus et al., 2004) leading to the suggestion (attribution) of an important role of sleep for memory consolidation. Most assumable, the mechanisms underlying the reported EEG-parameters are affected to a different degree by episodic and semantic memory encoding. This has not been studied yet. Thus, no inferences can be drawn on the existence of differential effects that sleep could have on episodic compared to semantic memory. In EEG as well as PET studies different activity patterns are found for episodic compared to semantic memory. This is not true for the cued recall performed immediately after encoding, after eight hours of sleep as well as one week after encoding. On the basis of such differential effects on the distinct memory systems found in behavioural data, we propose systematic comparisons of sleep EEG separately for episodic and semantic encoding.

The Watch-PAT100 includes pulse oximetry, PAT probe and actigraphy sensors. Data collected during the night were analysed automatically using the Watch-PAT dedicated software package that provided information on Respiratory Disturbance Index (RDI), oxygen desaturation index (ODI), arousal index (ARI) and sleep duration. Final diagnosis and treatment decision were made by a multi disciplinary team based on these results as well as clinical impression.

Results: 12 out of the 260 case were discarded from the study, because of technical difficulties with PAT probe sensors (N=11), and arrythmia that interfere with the recordings (N=1). In 28/248 cases the Watch-PAT100 results were inconclusive and a full PSG was needed in order to reach a final diagnosis.

In 220 cases, the Watch-PAT100 results were sufficient to establish the a final diagnosis and to decide on the mode of the treatment.

Given the facts that a full PSG requires 30 minutes of patients preparation and 60 minutes of data scoring and interpretation, using the Watch-PAT100 results in a considerable time and cost saving.

Conclusion: The Watch-PAT100 results in 84% reduction in full PSG studies which represents a considerable cost and time saving.

P 203
Possibilitys of professional intervention by health care professionells as nurses to support diagnosis of a patient with sleep/wake disorders

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Introduction: In the sense of an integrated care it is not, if the case happens that a patient become released some weeks before its renewed reception on an surgical ward, but he now accident suffered, because his sleepapnea syndrome was not recognized! Diagnosis in sleep medicine is based on a lot of automatically and apparatuses technology. So the question was: could the nurses as health care professionals with more contact to the patients intervene and which possibilities do they have?

Methods: First of all, all possible measures where collected and checked. As next those were filtered out which are not available to observe or measure (by human ability) sleep and wake behaviour with it.

Result: With 6 different methods it is possible to asses 19 different parameters of sleep/ wake behaviour with the help of the nurses.

Discussion: The nurses could complete with there knowledge and ability’s the diagnosis process. But there exist no uniform recommendations or guidelines for the health care professionals, to document and for Intervention. The next question should be if after an special educational training for nurses the diagnostic process could be more effective.

P 204
Examination for finding an optimised method for nurse documentation of sleep/wake behaviour

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Introduction: After discovering that detailed documentation about sleep wake behaviour is important and necessary as a base of intervention for nurse is clear there should be an accepted known method. Understandable for all parts during the diagnosis process. There exist many methods and systems for documentation, but there is unfortunately still no accepted protocol-paper for the objective assessment of sleep/ wake behaviour, for nurse documentation.

Methods: Collection of all conventional available documentation material compare and check it for the following developed criteria: comprehensive, evident, compatible, comparable, clear, easy to handle, obvious easy to understand....(at all where created 13 different criteria).

Results: The founded and checked material does not correspond to the Criteria. In general (material for) the objective assessment for the health care professionals as nurses are lacking. The result was motivating the Author to develop an Instrument for documentation and also an educational training for nurses which should be summarized in a Book as a “working-book” which should be published until the End of the year 2005.

P 205
Development of a patient training to the avoidance of injuries and injury falling as a result of loss muscletone in narcolepsypatients

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Introduction: As a consequence of the Cataplexy, frequently appearing slumps, sudden falls and accidents of other type are. The compensation behaviour of the patients leads to push through, almost automatically in addition, the knees at the beginning of the appearing muscle weakness. That itemizes in addition, that the concerned remains stand and at least with slope body. That takes a few seconds or minutes for the patient to wait in this position until it is possible to arrange itself again. In addition it is necessarily to concentrate the last
muscle power for to held the position to protect falling. Rarely it does not happen that the concentration will be disturbed. However, that the events in the background the concentration of the patient, appears so that he is no longer able to avoiding slump. The slump in that connection at the above mentioned compensation behaviour with “pushed through knees” results, is especially hard because the patient can fall no longer on the knees and cannot lift always its hands to the protection of the face.

Methods: ascertainment of a suitable “case trainings” to the injury prophylaxis, to the shortening or avoidance of rehabilitation and injury sequence. Comparison of conventional methods of case training. Confessed are case training natured out of the sport areas: battle sport, ride sport, skate sport…. Comparison of different “movement apprenticeship”: “Feldenkrais” methode, Kinaesthetic.

Results: that case training natured out of the sport do not suit require corresponds stands itself because it just a body tension to the execution that not the slight Muscle tonus that to the decree to the concerned in the moment. To be sure some movement flows suit themselves out of the apprenticeship of the Aikido, as well as out of the Kinaesthetic, that adapt itself the body physiology. Because the loss of muscle tone happens sometimes very fast and suddenly, the body changes his position very quickly, that seems to be suitable to take the recognitions out of the Kinaesthetic around a movement apprenticeship for the case of the trap from that. With a trial group Narcoleptic Patients out of the patient union the German Narkolepsie association already first trainings were tested and were perceived by almost all as an enrichment and progress. Further studies should show and confirm the effectiveness on safety, functionality and practicability in everyday life situations as well as reduction of the injury sequence and at least life quality.

P 206
The snoring and obstructive sleep apnea: diagnostic and efficacy of treatment evaluation

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Material and methods: There were examined 162 patients (among them 63 patients with snore examined before and after operation, and 99 patients with obstructive sleep apnea), (male-132, female-30, age from 21 to 64 years). All Pt has been undergone a respiratory monitoring during the sleep (screen system SC20 & CPAP PV 10i Breas device) and rhino-pharyngo-laryngoscopy (fiberscope “Pentax”, FNL-10-RBS) with functional tests (in sitting and lying position). And also pt and there sleeping partners have filled special forms before the operation and 2 month later. Polysomnography has been used two times for prognosis evaluation of obstructive sleep apnea treatment.

Cardio Respiratory Monitoring in a few cases has been used with blood pressure monitoring. It allowed to find out the correlation between blood pressure data and degree of respiratory disorders during the sleep in 25% of cases, and then with the help of CPAP therapy to reach reliable hypotensive effect without any changes in drug therapy.

The phenomenon of increasing of snoring intensity and syndrome of obstructive sleep apnea was described in patients with complicated snore and syndrome of obstructive sleep apnea (light level) who had been just operated in the nasal cavity (septum-operation, vasotomy), without following pharyngoplasty. Cardio Respiratory Monitoring is the method of choice for evaluation of different modifications of surgical treatment of soft palate and pharynx, including laser when complicated and uncomplicated snoring, and pharyngoplasty-light type of syndrome of obstructive sleep apnea.

Conclusions: Based on the mentioned-above data it is possible to suppose that surgical treatment, which were performed in the patients with snoring (> 5 years) and syndrome of obstructive sleep apnea (light and middle stage) as an independent method is not always bringing positive results. These operations in the nasal cavity should to be the first preparatory step of the surgical treatment of snore and syndrome of obstructive sleep apnea.

P 207
Automatic Detection of Sleep-Related Breathing Disorders is Possible by Transthoracic Impedance Recording Integrated into a Holter ECG System

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Background: Sleep-related breathing disorders (SRBD) demonstrate a high degree of coincidence with cardiac diseases (e.g., heart failure 82%, hypertension 30%, coronary artery disease 30–50%, pulmonary hypertension 9–37%). Effective treatment of sleep apnea accordingly results in improvement of cardiovascular function and prognosis. Widespread screening for SRBD in this patient group is consequently desirable. We evaluated an algorithm to detect nocturnal apneas in accordance with transthoracic impedance (TTI) changes, by a signal additionally recorded in a Holter ECG (CardioMem 3000®, the getemed company).

Methods: We examined 180 outpatients (79% male; mean age 55.5) by routine diagnostics, including recording by Holter ECG, but with integrated transthoracic impedance recording (CM3000®, the company getemed, in Teltow, Germany). We simultaneously per-formed standard
polygraphy with a validated sleep-apnea screening tool (ApnoeScreen®, JAEGER). In blinded mode, we compared the findings from automatic impedance analysis (I-AHI, see above) with the results from standard polygraphy (AHI). We then calculated a correlation index to assess the sensitivity and specificity of this new method in screening for sleep apneas.

Findings: Through sleep-apnea monitoring we determined that 46 of the patients studied demonstrated an apnea-hypopnea index (AHI) of >10/h (prevalence = 25.5%). For 37 of these 46 patients, automatic analysis of the impedance signal disclosed an I-AHI >10/h (sensitivity = 80%). Only 9 out of 133 patients without SRBD were false positive (specificity = 93%).

Conclusion: Automatic detection of sleep-related breathing disorders (SRBD) is feasible through integration of transthoracic-impedance-recording into a Holter ECG system. This new additional method of apnea screening demonstrates satisfactory sensitivity for detection of SRBD, and exhibits high specificity to prevent false positive findings in patients without SRBD. Further studies are necessary to evaluate this system under conditions of everyday life.

P 208
Cognitive Effects of Armodafinil in Patients with Excessive Sleepiness and Obstructive Sleep Apnea/Hypopnea, Narcolepsy, or Shift Work Sleep Disorder

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Aims: This analysis of data from four phase 3 clinical trials was performed to assess the effect of armodafinil, the R-enantiomer of modafinil with a longer half-life, on cognition in adults with excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome (OSAHS), narcolepsy, or chronic shift work sleep disorder (SWSD).

Methods: The efficacy and safety of armodafinil (150 mg and 250 mg) were assessed in four 12-week randomized, double-blind, placebo-controlled, parallel-group trials in patients with excessive sleepiness associated with OSAHS (2 studies), narcolepsy (1 study), and SWSD (1 study). In addition to sleepiness and fatigue assessments, memory and attention were assessed in all patients using the Cognitive Drug Research (CDR) computerized assessment system at baseline and weeks 4, 8, and 12. CDR testing comprised 3 tests of attention and 5 tests of memory from which 4 composite variables were derived: power of attention; continuity of attention; speed of memory, and quality of episodic secondary memory. On each visit, CDR testing was performed at 2-hour intervals (between 0930 and 1930 for OSAHS and narcolepsy and between 0230 and 0830 for SWSD). Data presented are the average of first 4 test sessions.

Results: Data from 981 patients who received armodafinil 150 mg/day, armodafinil 250 mg/day, or placebo were included in this analysis-599 patients in the OSHAS trials (n = 235, n = 121, n = 243, respectively), 173 in the narcolepsy trial (n = 57, n = 59, n = 57, respectively), and 209 in the SWSD trial (150 mg/day, n = 109; placebo, n = 100). The CDR memory tests identified a consistent effect of armodafinil to improve the quality of episodic secondary memory. Mean (SD) changes from baseline were 10.9 (31.0), 9.8 (32.2), and -0.7 (46.3) in the armodafinil 250–mg/day, 150 mg/day and placebo groups, respectively in the combined OSA/HS studies (armodafinil 150 mg/day vs placebo; p < .01); 18.4 (38.3) and -3.3 (39.6) in the armodafinil 150 mg/day and placebo groups, respectively in the SWSD study (p < .001); and 16.5 (46.5), 20.7 (34.5), and 1.0 (29.1) in the armodafinil 250 mg/day, armodafinil 150 mg/day, and placebo groups, respectively in the narcolepsy study (p < .05). The CDR attention tests identified significant improvements in the power of attention in patients with narcolepsy (p = .0498) and SWSD (p = 0.0011). No consistent effect of armodafinil on attention was observed in the OSAHS population. Armodafinil was generally well tolerated in all 4 studies. Headache was the most common adverse event reported in all patient populations.

Conclusions: Armodafinil provides significant improvements in attention in patients with excessive sleepiness associated with narcolepsy and SWSD and memory in all populations evaluated.

Animal Models

P 209
Biperiden-induced delirium model in rats: behavioral and electroencephalographic study

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Aims and Methods: In order to elucidate the neurological mechanisms of delirium, we administered the anticholinergic drug biperiden (40 mg/kg i.p.) to 10 adult male Wistar rats and examined the resulting polygraphic recordings (electroencephalography, electromyography, and electror- oculography) for 2 h following injection. Ten male Wistar rats receiving saline (i.p.) were used as the control group.

Results: Treated rats alternately demonstrated two types of behavioral change: hyperactive and hypoactive states. In the hyperactive state, rapid walking, excessive random searching, rearing at walls and retropulsion were observed, with marked rapid eye movements, and increased delta and alpha-1 band electroencephalography activity. In the hypoactive state, motor arrest and drowsiness were observed, with mild rapid eye
movements, increased delta band and decreased alpha-1 and theta-2 band electroencephalography activity, and mild electromyography activity. On the other hand, the control group rats did not show any behavioral or electroencephalographic changes.

**Conclusions:** The behavioral and electroencephalographic changes induced by biperiden administration in rats are similar to those of delirium in humans. Therefore, it is suggested that the biperiden-treated rat is a good delirium model and anticholinergic mechanism is one of the potent factors of the development of delirium in humans.

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**P 210**

**Role of lateral Orbitofrontal cortex in duration and time of sleeping**

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Sleep is a biological rhythm that is controlled by many structures and neurotransmitter systems in brain. Previous evidences suggested that Orbitofrontal Cortex (OFC) probably involved in sleeping time and duration.

The aim of this study is determine of the role of lateral OFC area in duration and time of sleeping by electrical lesions. Male Wistar rats (220–250 gr) used in this experiment. Rats were surgically implanted bilaterally guided cannulae aimed at the Lateral OFC by stereotaxic instrument. One week after recovery at first the sleeping assessed by behavioral methods and then lateral OFC lesioned by use of lesion-maker (electrical electrode) and measurement of behavioral manifestations continued in the time and sleeping duration.

Results indicated that electrical lesion of Lateral OFC significantly increased sleeping time (P < 0.01).

Our Findings showed that Lateral OFC of rat’s brain may be play important role on the regulating of sleep.

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**P 211**

**The effect of Portulaca Oleracea and Melissa Officinalis extracts on sleeping time in Mice**

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Previous evidence suggested that medical plants especially Portulaca Oleracea (PO) and Melissa Officinalis (MO) probably involvement in sleeping time and duration. The aim of this study was determine the effect of FP on sleeping time on mice.

Male albino mice (25–30 gr) rats were used in this study. The animals divided into control (saline) and treatments groups. For measuring of sleeping time we used of Angle method by trans-user and physiograph. For assessment of effects of PO and MO we used of different doses of those [PO (25, 50 and 75 mg/kg) and MO (5, 10 and 25 mg/kg)] by IP injection 30 min before of observation or assessment of sleeping time and duration.

The results indicated that of PO and MO significantly increased sleeping time and duration (P < 0.05). Finding above showed that PO and MO that may plays important role on the modulation of sleeping time.

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**Animal Studies**

**P 212**

**Changes in REM-sleep theta-peak frequency in SHARP-1/SHARP-2 double null-mutant mice**

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**Introduction:** The basic helix-loop-helix (bHLH) transcription factors SHARP-1 (DEC2/BHLHB3) and SHARP-2 (DEC1/Stra13/BHLHB2) are rhythmically expressed in neurons of the central circadian pacemaker residing in the suprachiasmatic nuclei (SCN) of the hypothalamus. Previous studies analysing the circadian phenotype of SHARP-1 & -2 deficient mice by monitoring wheel running activity suggest an important role for both genes in the regulative mechanisms underlying the adaptability of the endogenous clockwork to external time. The aim of the current study is to analyse changes in sleep behavior in SHARP-1 & -2 double null-mutant mice (SCKO) compared to wildtype (SYKO) mice.

**Methods:** male SCKO (n=5) or SYKO (n=7) were housed under a constant 12:12 h L:D cycle with food and water ad libitum. Four steel screws for EEG- and two steel wires for neck-muscle EMG recording were implanted under deep ketamine/xylazin anaesthesia. After two weeks of recovery EEG/EMG were recorded for 48h starting with light on. Wakefulness (w), rapid-eye-movement (REM) sleep and non-REM (NR) sleep were classified in 4s epochs offline by visual scoring. Fast-fourier-transformation (FFT)-spectral-analysis was performed for each stage and after exclusion of artifact- disturbed epochs averaged for two-hour intervals. Although still in progress, the analysis was restricted to the first two hour intervals (following light onset) so far.

**Results:** There are no significant changes concerning the distribution of W, NR and REM in the first two hours of recording. However, FFT-analysis revealed a significant difference in the theta-peak-frequency between wildtype
The Effect of High Doses of Naloxone on the Sleep-Wakefulness Cycle

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Aims: Endogenous opioid peptides act as neuromodulators, which modify the action of other neurotransmitters in the central nervous system. Endogenous opioid peptides can influence the release of various neurotransmitters. As a result of this modulation, opioid peptides can affect certain physiological states, including mood and sleep. Opioid receptors are found in various brain structures involved in Sleep-Wakefulness Cycle regulation. It is generally known that exogenously administered opiates and opioid peptides can alter sleep pattern. The doses of Naloxone (Naloxone Hydrochloride) necessary to influence Sleep-Wakefulness Cycle are much higher than those necessary to antagonize the other effects of opiates, whereas morphine doses capable of altering Sleep-Wakefulness Cycle are relatively small. However, endogenous opioid peptides have greater affinity for opioid receptors than exogenous opiate agonists or antagonists, and the discrete brain localization of specific opioid peptides raises the possibility of differential effects between exogenous opiates and endogenous opioids. The aim of the presented work was to study the influence of endogenous opioid peptides on the Sleep-Wakefulness Cycle structure by blocking of opioid receptors. For this purpose we used high doses of Naloxone nonselective opioid receptors antagonist.

Methods: The experiments were conducted in Mongrel adult male rats (n=5) weighing 330–380 g. After adaptation period electrodes were implanted into different cortical areas: sensorimotor and dorsal hippocampus projection of the cortex, oculomotor and neck muscles under chloral hydrate anesthesia. After complete recovery the animals were i.p. injected with different doses of Naloxone (10 mg/kg; 20 mg/kg). EEG registration of Sleep and Wakefulness was continued until background cycle was restored. Sleep-Wakefulness Cycle was recorded during 7 hours. The data were statistically evaluated and treated by Student’s t-test.

Results: High doses of Naloxone administration resulted in changes of the Sleep-Wakefulness Cycle structure.

Naloxone produced a dose-dependent increase of the Deep Slow-Wave Sleep (DSWS) from 24% (background condition) to 29% (Naloxone 10 mg/kg) and 32% (Naloxone 20 mg/kg). During the DSWS delta and sub-delta waves ratio changed-delta waves decreased and sub-delta waves increased after high doses of Naloxone administration in comparison with background indices. With regard to the Paradoxical Sleep we found no decrease in percent amount of these stage referred to the whole cycle.

Conclusions: These findings indicate that high doses of Naloxone may act indirectly by blocking of opioid receptors located on other neurotransmitter cells, which mediate Slow-Wave Sleep. It is suggested that endogenous opioid peptides may be involved in the regulation of Sleep-Wakefulness Cycle.

Down-regulation of Neuronal NADPH-d/NOS Expression in the Vagal Afferent Neurons of Total Sleep Deprived Rats

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Aims: Nitric oxide (NO) plays an important role in the regulation of cardiorespiratory function. Since sleep disorder is commonly associated with substantial cardiorespiratory disturbance, the present study is aimed to determine the NO synthase (NOS) expression in the vagal afferent neurons following total sleep deprivation (TSD).

Methods: Quantitative nicotinamide adenine dinucleotide phosphate-diaphorase (NADPH-d) histochemistry along with neuronal NOS immunofluorescence were used to examine the NOS reactivity in adult rats subjected to five days of TSD.

Results: Results indicated that in normal un-treated rats, numerous NADPH-d/NOS reactive neurons and fibers were found in nodose ganglion (NG) and dorsomedial (dm), medial (m), parvocellular (pv) and commissural (com) subnuclei of nucleus tractus solitarius (NTS). However, following TSD, both the percentage and staining intensity of NADPH-d/NOS reactivity were drastically reduced in NG and all above-mentioned subnuclei of NTS than that of normal un-treated ones.

Conclusions: Concerning NO could serve an important sympatho-inhibitory messenger released by vagal afferent neurons, decrease of NOS expression may impede the
processes of NO production and contribute to the formation of TSD relevant cardiorespiratory disturbance.

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**Coronary Blood Flow Increases with Obstructive Sleep Apnea but Becomes Dissociated from Myocardial Work Following Lipopolysaccharide Infusion**

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**Introduction:** Obstructive Sleep Apnea (OSA) is associated with an increased prevalence of ischemic heart disease and a poor prognosis in long term follow up. The mechanisms underlying these associations are uncertain, but are likely to involve altered regulation of coronary artery blood flow (CBF). The endothelium is an important regulator of blood flow. Endothelial dysfunction has been identified as a crucial component of atherosclerosis, but as yet its potential effects on CBF during OSA is unknown. We hypothesized that in states of endothelial dysfunction, there will be abnormalities of CBF regulation during OSA that may predispose patients to adverse outcomes.

**Aims:** To measure CBF changes with OSA before and after endothelial damage with lipopolysaccharide infusion, and to explore its relationship to myocardial work and O2 desaturation.

**Methods:** Newborn lambs (n=5) were instrumented under general anesthesia for recording CBF (Transonic™ flow probe over circumflex coronary artery), arterial pressure (Pca), left atrial pressure (Pla), central venous pressure (Pjv) and sleep monitoring (bio-electrodes). At a second operation, a modified tracheostomy was inserted to allow control of the upper airway. Following recovery, a baseline sleep study was performed during which OSA was modeled by manually occluding the tracheostomy repeatedly during sleep. Endothelial damage was then induced by infusing lipopolysaccharide (LPS, 2 µg/kg) on 3 successive days. A second sleep study was performed the next day with repeated OSA. Hemodynamic and sleep data were continuously recorded throughout both sleep studies. Myocardial work was noninvasively determined using the heart rate-blood pressure product (RPP).

**Results:** The conditions of study were the same pre and post LPS treatment. SaO2 min with OSA was 90.7 ± 2.36% (mean ± SEM) pre LPS, with no significant difference post LPS exposure. Following termination of OSA, mean ΔCBF was 9 ± 2% above baseline, both before and after LPS treatment. Determinants of the ΔCBF rise were assessed using forward stepwise multilinear regression analysis. Prior to LPS infusion, significant predictors of ΔCBF at apnea termination were RPP (r²=0.50), SaO2min (r²=0.11) and arousal (r²=0.04), all p<0.01. Following LPS infusion, degree of O2 desaturation was the only significant predictor of ΔCBF (r²=0.14, p<0.05).

**Conclusion:** CBF increases at the termination of obstructive apnea and is normally closely correlated with the degree of increase in myocardial work. After exposure to LPS, there is uncoupling between myocardial work and CBF at the termination of obstructive apnea. These results suggest impaired coronary blood flow-metabolic coupling during states of endothelial dysfunction.

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**Architecture of the Sleep-Wakefulness Cycle Following New Strategy of REM Sleep Deprivation**

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**Aims:** Since the discovery of REM sleep (REMS), various techniques of its deprivation are used in basic and clinical sleep research. However, most of REMS deprivation procedures lead to progressive REMS propensity increase that perhaps is the reason for the mood deterioration of depressive patients in postdeprivation days. Our previous studies have demonstrated the possibility of REMS full elimination from sleep-wakefulness cycle without accumulation of REMS need through partial substitution of slow-wave sleep (SWS) by active waking episodes. Here we evaluate the variation occurring in the postdeprivation sleep-wakefulness cycle in cats.

**Methods:** Adult male cats (n=8) were implanted with chronic electrodes for the registration of sleep-wakefulness cycle. After recovery from the surgical trauma and adaptation to the experimental set sleep-wake states were recorded during a 24-hour baseline and partial SWS deprivation sessions followed by 24-hour of postdeprivation period. Total amount, frequency, percentage ratio of sleep-wake states and latency of sleep stages as well as heart rate, PGO-spikes and rapid eye movements frequency during REMS were calculated and compared with corresponding baseline data. Differences were assessed using paired student’s t-test.

**Results:** In postdeprivation protocol, amount of wakefulness was far less than baseline levels, whereas total SWS time increased significantly. Neither REMS pressure nor its rebound was observed in various postdeprivation time intervals. Although SWS latency was shorter in comparison to baseline protocol, there was significant increase of REMS latency in the postdeprivation cycle. Heart rate and number of PGO-spikes during postdeprivatin REMS episodes did not differ from baseline data, however an obvious decrease of rapid eye movements frequency was detected.

**Conclusion:** Neurophysiological analysis of results allows to conclude that partial SWS substitution by active
wakefulness is not followed by enhancement of REMS either in quantity or quality. It is suggested that a new selective REMS deprivation strategy elaborated in cats may be examined on humans.

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**Laminar organization of spindle oscillations in somatosensory cortex during wakefulness and early stages of sleep in rat**

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**Aim:** Investigation of spatiotemporal organization of spindle oscillations in the upper and lower layers of somatosensory cortex and within the specific and nonspecific thalamic nuclei.

**Methods:** Registration of spontaneous and electrically induced focal activity in 30 partly immobilized by *d*-tubocurarine chloride adult rats during wakefulness and early stages of sleep (method is approved by Committee of Bioethics of the Russian Academy of Science). The recording and stimulation were performed by glass microelectrodes (tip resistances ~1–2 MΩ) placed stereotaxically in specific (VPL, VPM) and nonspecific (intralaminar group) thalamic nuclei, and within the supragranular (I–III) and infragranular (V–VI) layers of the primary somatosensory (S1) cortex. Frequency-modulated electrical threshold stimulation was applied to specific and nonspecific thalamic nuclei. The checking of current functional state of animal during the wakefulness and initial stages of sleep was realized on evoked bioelectrical activities, electroencephalogram, electrocardiogram, as well as on a motor activity of vibrissae. The statistical spectral analysis: spectrums of powers, coherency and phase cross-correlative spectrums were used.

**Results:** The shape, dynamic and amplitude of evoked responses, as well as the phase relations of the thalamic and cortical spontaneous and evoked rhythms were analyzed. The state of wakefulness was characterized by the high level of the brain activations that expressed in domination of theta-rhythm activity as in lower (V–VI) layers of somatosensory cortex, so and in thalamus. During the transitions to early stages of sleep, there was occurred the suppression of the theta-rhythm in a cortex and thalamus and appeared the typical spindle activity. In the initial stages of sleep, the phase shifts of spindle oscillations between thalamus and both upper and lower cortical layers were observed. At the same time, the coherency of the spindle oscillations in the thalamic nuclei and lower cortical layers was higher than coherency in the upper layers, what indicates to the prevalence of the corticofugal influences.

**Conclusions:** (1) In the wakefulness exists higher level of the cortical and subcortical activation, than in somnolent states, which reveals, in particular, at the domination of the theta-rhythm activity in lower layers of the somatosensory cortex. (2) In the initial stages of sleep, the infragranular layers of the primary somatosensory cortex functionally are closer with a thalamic nuclei than the supragranular layers.

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**The effect of Ferula Persica extract on sleeping time in Mice**


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Previous study indicated that sleep controlled by many factors in the brain and some drugs especially medical plants probably involvement in sleeping time and duration. The aim of this study was determine the effect of extract of Ferula Persica (FP) as a medical plant on sleeping time in mice.

Male albino mice (25–30 gr) rats were used in this study. The animals divided into control (saline) and tests (drug) groups. For measuring of sleeping time we used of Angle method by trans-user and physiograph. For assessment of effects of FP we used of variant of doses (50, 100 and 200 mg/kg), that injected IP 30 min before of observation or assessment of sleeping time.

The results indicated that extract of FP significantly effect on sleeping time and increased that in comparison with control group (P < 0.01).

Finding above showed that FP that may be play important role on the modulation of sleeping time and duration.