

## DOES EARLY IRON DEFICENCY ANEMIA INTERFERE WITH CHILDHOOD REM SLEEP ORGANIZATION PATTERNS?

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*Introduction:* The establishment of the sleep/wake cycle and the internal architecture of sleep are fundamental steps in the neurofunctional maturation of the brain. Lasting abnormalities in sleep/wake and activity rhythms have been reported in IDA rodents, but are yet to be explained. It is known that iron is required for the functioning of several neurotransmission systems, myelination, and neuronal metabolic activity; thus, different processes may be related to their alteration. Since one of the main sleep organization changes during early infancy is the reduction and temporal distribution of REM sleep, we evaluated whether early IDA would provoke long-lasting effects on nocturnal REM sleep organization.

*Methods:* All-night polysomnographic recordings were done in a group of healthy 3- to 4-year-old children who were treated for IDA (n=24) or were nonanemic (controls, n=26) in infancy. NREM stages III and IV were grouped as SWS. The duration of each SWS and REM sleep episode was analyzed according to each successive third of the night.

*Results:* Between groups, REM and SWS episodes were differently distributed throughout the night. The pattern of REM sleep episodes was different between groups: in controls, the duration of REM episodes increased with advancing thirds, while in former IDA children the duration was similar in all thirds. Furthermore, former IDA children demonstrated a short latency ( $p<0.02$ ) and a consistent tendency for a long duration of the first REM episode.

*Discussion:* Altered nocturnal temporal organisation of sleep patterns in former healthy IDA children suggests that iron is essential for the normal progression of sleep patterns. Several characteristics of REM sleep organisation in former IDA children indicate that neurodevelopmental processes do not follow age-related expected modifications. It is conceivable that the disruption of REM sleep temporal patterns represents an underlying mechanism that interferes with optimal behavior during both sleep and wakefulness. In fact, REM sleep patterns are reminiscent of those often observed in young depressed subjects and could be related to the depressive symptomatology observed in former IDA subjects during adolescence.

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## RESTLESS LEGS SYNDROME: CLINICAL EXPERIENCE WITH LONG-TERM TREATMENT

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*Introduction* There are almost no data on both long-term treatment efficacy (<sup>3</sup> 6 months) and predictors of good treatment response in patients with restless legs syndrome (RLS) outside study protocol conditions. The value of a newly described RLS score (RLSS; [2]) for assessing severity and changes of severity of RLS symptoms is unknown.

*Methods* Over three years 70 RLS patients (pts; 36 men, 34 women; mean age of 59 years, range 29-79) were prospectively studied and seen at least twice in our sleep clinic. Diagnosis of RLS was made according to international criteria [1]. Clinical and polysomnographic data as well as severity of RLS symptoms, as estimated by RLSS, were assessed at study begin. Periodic limb movements in sleep (PLMS) were scored according to conventional criteria. Patients were treated on an individual base. After a follow-up time of 1-106 months (mean=16; 51 pts <sup>3</sup> 6 months, 64 pts <sup>3</sup> 3 months) RLS symptoms were re-assessed by both overall clinical impression (much better, better, unchanged, or worse as compared to study begin) and RLSS. Clinical characteristics and treatment response were compared between naive pts (N, never treated for RLS before study begin) and pts with previous treatment for RLS (T). Predictors of treatment response were searched for comparing pts with good treatment response (G, much better or better on follow-up) and those with bad treatment response (B).

*Results* At follow-up 76% (30/40) N-pts and 77% (23/30) T-pts had a good treatment response. No significant differences were found between the two groups in age, gender, etiology and duration of RLS, familiarity, presenting sleep complaint, RLSS, and percentage of pts with PLMS. PLMS were more common in B- than G-pts (100% vs 58% of pts, p=0.008). In all other variables considered G-pts and B-pts did not differ significantly. In all 70 RLS pts the mean RLSS was 26 (range 12-38) at baseline 19 (range 1-36) at follow-up. There was a significant correlation between improvement of overall clinical impression (better or much better on final follow-up) and reduction of RLSS (p<0.01). Two patients had previously unknown „sleep attacks” while taking pergolide (2mg/die) and pramipexole (0.5mg/die) respectively. These episodes disappeared when medication was tapered off (pergolide) or reduced (pramipexole 0.25mg/die).

*Conclusion* 1) A good long-term treatment response can be obtained and maintained in a clinical setting in about 80% of RLS. 2) Patients without PLMS have a better long-term treatment response. 3) The RLSS represents a useful tool for assessing changes in severity of RLS symptoms in individual patients over time.

## WORK ACCIDENTS RELATED TO SLEEPINESS

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There are many papers about the sleepiness related traffic accidents. We have study the sleepiness as reason of accidents in the work area, including the itinerary from home, hours of work and hours of sleep and rest. We considere as work accidents simple sharp injuries, with or without suture, traumatismos with contusion, tumbles, fractures, sprain milds and severes, craneal trauma (with o withouth unconciousness). We study 649 patients: Morning Shift: 342; Afternoon Shift: 162; Night Shift: 135. The occurrence of accidents was analyzed having in mind: a) hypoglucemia by prolonged fasting, insuficient nutrition, sleepines and poor sleeping. b) poor rest, daily routine, excessive and obsesive working, multiples activities, fast rythm, personal, famiial and labour problems. Variability in accidents horary was observed in thre three shifts and related with different reasons from our point of view. We concluded that this is a great problem to solve, because the consecuenes affect as the workers as the owners and more information is necessary about the cost of this accidents.

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## INCIDENCE OF EATING HABITS AND SLEEP SCHEDULES IN PATIENTS WITH INSOMNIA AND SNORING

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The majority of the patients seen in our Sleep Laboratory are suffering from insomnia and snoring. Excessive daytime sleepiness (EDS), cognitive disturbances and mood changes are the most common symptoms. In order to evaluate the eating habits and sleep schedules for those patients they filled out a self-reported questionnaire previously the performance of another diagnosis studies.

Based on the self-reported questionnaire results, we asked the patients to reduce the amount of night meals and to extend the time before going to bed.

To establish if the eating habits (meals time and amount) and the time between the last meal and the sleep onset it has incidence on the patients reported sleep quality.

Simple questionnaire with a graphic was made in order to asses: a) bed time and awaking time, b) meals time, c) amount of every meal (B-L-D)

Over a total of 1600 patients we selected 923 (349 women and 574 men [ 563 patients with snoring – with or without apneas- and 360 patients with maintenance insomnia]). Age ranges: 22 to 86 years. All of them live in Buenos Aires City and its area round.

The amount of food was classified as: No meal, Light meal, Normal meal and Heavy meal.

The time between the last meal and the sleep onset was recorded in hours and minutes.

The selected patients completed the questionnaire under our supervision. We found that 82 % of them take Normal and Heavy dinner, 68 % take Light or No breakfast. All of them lasted less than 3 hours to get the sleep onset. 38 % of the patients lasted 90 min and 48 % 120 min. With the prescription of reducing the night meal and extending the time previous to going bed, 57% of the patients showed less EDS, better quality of sleep and improvement of the cognitive disorders and mood changes.

We think that those results confirm the importance of the “digestion rol” during the sleep on the origin of these sleep disorders : insomnia and snoring.

This is part of a larger research involving the motives that causes these alterations.

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## EFFECT OF GASTROINTESTINAL DISEASES ON INSOMNIA AND SNORING

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The influence of gastrointestinal activity during the sleep have had examined in recent international publications. The International Classifications of Sleep Disorders and several papers confirmed that gastroesophageal reflux disease (GERD) and duodenal ulcer (UD) may disturb sleep.

We studied 100 patients, over a total of 578 (41Females,59Males), age ranges 22-75 years. They were were recruited between 1996-2000.

We found a hight frecuency of excesive daytime sleepiness (EDS), psychosocial problems, attention-deficit and cognitive disturbances, specially in the snoring patients.

BMI (Body Mass Index) was an important sign to consider in this group of patients. PSG was realized in 71 snoring patients and 4 insomniacs. 99 subjets underwent gastrointestional roentgenologic study with double contrast . 11 cases had endoscopic digestive study. The endoscopic evaluation of upper airways was made in 66 snoring patients. The PSG showed Apneas and Hypopneas in 47 snoring patients. The Apnea-Hipopnea Index (AH/I) was normal (behind 10) in 28 cases; mild in 25 patients, in 22 moderated and in 10 of all was severe.

The endoscopic study of upper airways examination determinated acid laryngitis in 46 cases. The gastrointestinal roentgenologic evaluation showed hiatal hernia in 87 and GERD in 84 patients. The endoscopic digestive study confirmed the esofagyitis and GERD in all of cases. We found a better quality of sleep in the patients who reported GERD symptoms with the prescription of reducing the nighth meals and promotions of health food. The most of the patients (85/100) reported an improvement of their main symptoms (e.g. insomnia or snoring) and increased the welfare when the specific therapy was administrated (omeprazol, lanzoprazol). In this study we found a significant association between gastrointestinal disorders and Insomnia and Snoring.

Our findings suggest that education and promotion of healthy eating habits and the righth digestive assess should be advocated in addition of the traditional treatment of this common sleep disorders.

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## SLEEP DISORDERS IN PATIENS WITH DOWN SYNDROME

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*Introduction:* Sleep disorders have important impact on the quality of waking life for children and adolescents.

Patients with Down syndrome are a risk group for disturbed breathing during sleep due to their structural characteristics affecting upper airway size.

Children with attention deficit disorders show sometime behavior disorders that can be related to sleep pathology.

The aim of the study is to know the existence of sleep disorders on patients diagnosed as having a Down syndrome and their repercussion over wake time.

*Material and Method:* Three pages screening questionnaire was administered to parents of Down syndrome patients and for comparison siblings of patients Down syndrome. The questionnaire included 14 items that focused on medical and structural characteristics, 12 items related to sleep behavior and 7 items related to daytime behavior.

Both groups results were compared and showed significant statistical differences in open mouth during sleep, noisy breathing, nocturnal snore, legs movements, stand up on bed and observed apneas.

	Down S. Group		Control Group		p
	Yes	No	Yes	No	
Observed sleep apneas	29	86	1	46	< .000
Nocturnal snoring	46	74	10	39	< .05
Sleep noisy breathing	53	88	10	30	< .005
Open mouth during sleep	82	38	12	38	< .000
Sleep legs movements	79	40	17	31	< .000

Key words: Down syndrome, sleep disorders, behavior disorders.

## CHANGES IN SLEEP QUALITY AMONG HIV POSITIVE INDIVIDUALS AFTER SIGNIFICANT CAFFEINE REDUCTION: ANALYSIS OF PITTSBURGH SLEEP QUALITY INDEX SUBSCORES

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*Introduction:* Sleep pattern disturbances in persons with HIV have been reported to be as high as 79%, far exceeding the proportion found in healthy populations. High levels of caffeine consumption may have an exacerbating effect on already prevalent HIV-related sleep pattern disturbances. Persons with HIV may have altered hepatic caffeine metabolism, possibly due to high rates of hepatitis co-infection and widespread antiretroviral hepatotoxicity associated with the many drugs taken daily in the management of the disease. *Purpose:* The purpose of this study was to test whether there were any differences in sleep between a group of persons with HIV (60% AIDS and 40% HIV+ only) who reduced their caffeine intake from baseline by 90% or greater for 30 days ( $n = 44$ ) versus a group of persons with HIV who continued their usual caffeine consumption ( $n = 44$ ). *Sample:* An international sample of 221 HIV+ subjects from the United States, Canada, and Brazil were recruited from print sources and the Internet and initially requested entry in the study. Of these, 88 subjects successfully completed either protocol. Each subject reported significant sleeping difficulties (mean pre-PSQI score = 11.06), taking antiretroviral medication, and consuming caffeine daily (mean mg/caffeine/day = 476). Mean CD4+ T cells were 423 and mean HIV Viral Load was 16,414 copies/ml, although 60% reported “less than 400” or “undetectable viral loads.” *Method:* An experimental design with convenience sampling and stratified random assignment was used. Subjects were administered pre- and post-test Pittsburgh Sleep Quality Index (PSQI) and MOS-HIV Health Survey instruments, with MOS-HIV summary scores used as a health status covariate. *Results:* Paired-samples T-tests found significant differences between pre- and post-PSQI subscores on measures of subjective sleep quality ( $p = .000$ ), sleep latency ( $p = .000$ ), sleep duration ( $p = .000$ ), sleep disturbances ( $p = .000$ ), use of sleeping medication ( $p = .001$ ), and daytime dysfunction ( $p = .004$ ) for experimental group subjects, and on measure of subjective sleep quality ( $p = .002$ ) for control group subjects. Overall, there was a significant difference ( $F = 14.032$ ,  $p < .001$ ) between the two groups on ANCOVA analysis for sleep, identifying a 35% improvement in sleep among experimental group subjects. *Conclusions:* The PSQI subscores which changed the most indicated that experimental subjects had improvements in subjective sleep quality, decreased sleep latency, and decreased occurrence of sleep disturbances. Significant reductions of caffeine may improve (though certainly not eliminate) sleep quality in persons infected with HIV.

## STRESS INFLUENCE ON SLEEP AND ABSENCE-EPILEPSY IN GAERS RATS

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GAERS rats (Genetic Absence Epilepsy Rats from Strasbourg) are defined as a genetic absence-epilepsy model, well known to exhibit spontaneous seizures characterised by generalised spike-wave discharges (SWD) (1). With this animal model, we previously showed that the SWD manifestation occurs mainly at the expense of paradoxical sleep (PS), while slow wave sleep (SWS) and wakefulness (W) are lightly modified (2). We also demonstrated that nitric oxide contained in brain, exerts an anti absence-epilepsy role and that the substances used in clinic ( valproic acid –VPA-) to treat this pathology might act through their ability to release the endogenous NO (2). Otherwise, it is also known that stress influences the duration and quality of sleep. In this respect, it has been reported that rats submitted to a short intense immobilisation stress exhibit immediately after, a sleep rebound characterised by an increase in SWS and PS duration (3). Finally, in epileptic patients, stress is also commonly believed to precipitate seizures.

According to the above data, the present study tried to better define the nature of the correlation existing between PS and SWD in GAERS rats. For this purpose, an immobilisation stress (IS) was imposed to GAERS rats treated or not treated with VPA.

Experiments were conducted on one-year old male GAERS and control rats. For polygraphic recordings, the rats were implanted under chloral anaesthesia, with EEG and EMG electrodes. After surgery, each animal was placed in an individual cage and kept in a sound attenuated room maintained at 22-24°C under a 12h/12h dark-light schedule. The 1-hour IS was performed by enclosing each naïve rat in a plastic tube at the beginning of the dark period. One group of rats was submitted to the IS while a second one received before the IS, a VPA injection (i.p. 200mg/kg). Polygraphic recordings were performed continuously over the 48 hours of the session including control and experimental periods.

The results obtained indicate that as long as control rats were restrained, SWS was strongly decreased and PS suppressed while in GAERS rats, the sleep loss was immediately replaced by seizures increase (+119%). This effect was not observed in the animal group treated with VPA (-38%). After the 1h IS, control rats exhibited a sleep rebound characterised by an increase in PS (+150%) and SWS (+132%), while in GAERS rats a decrease in PS (-75%) replaced by an increase in epileptic paroxysms (+110%) was observed. After pre-treatment with VPA, the IS did not induce changes in SWS of control rats while PS was significantly increased ( 6<sup>th</sup>: +63%; 18<sup>th</sup>: +34%). In GAERS rats, it is to be noticed that the magnitude of the changes regarding PS (-42%) and epileptic seizures (+16%) is less important after VPA followed by the IS than after the IS alone.

The results obtained on GAERS rats, indicate that stress exerts opposite effects on PS (decrease) and absence seizures (increase). The reduced magnitude of the effect on epileptic seizures observed after VPA treatment might be due to the ability of this compound to trigger an endogenous release of NO. Moreover, according to the tight but opposite relationships existing between PS and epileptic seizures, it appears likely that pontin structures generating PS, also containing a NOergic component (n. pedunculopontin and laterodorsal tegmenti), might be concerned in this respect. Finally, NO previously described as an antiepileptic free radical, might also possess anti-stress properties.

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COLLATERALS OF DOPAMINERGIC NIGROSTRIATAL PROJECTIONS  
INNERVATE THE THALAMUS AND DEGENERATE IN ANIMAL MODELS OF  
PARKINSON'S DISEASE

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The mesostriatal, mesocortical, and mesolimbic dopaminergic (DA) systems influence movement, cognition, emotion, and positive reinforcement. We identified a fourth major pathway originating from mesencephalic DA neurons: a mesothalamic system. Histochemical visualization of the dopamine transporter (DAT) was localized to thalamic regions known to modulate state, as well as motor and limbic related nuclei as opposed to sensory nuclei in rats, non-human primates, and humans. Immunoelectronmicroscopy identified a majority of axon terminals in the monkey reticular thalamus as DAT-immunoreactive (IR) (28 DAT-IR vs. 35 non-IR). Two DAT-IR profiles were juxtaposed to cell bodies, 5 to large dendrites, 16 to small and moderate-sized dendrites, 3 to other axons, and 2 were indeterminate. Eight made distinct synaptic contacts with symmetric morphology. Anatomical tracing established axon collaterals of the nigrostriatal pathway as the origin of this innervation. In contrast to the bilateral thalamic projections from the pedunculopontine nucleus (PPN) and the locus coeruleus (LC), the dopaminergic projections from the substantia nigra pars compacta (SNc), as well as parallel projections from non-dopaminergic SNc cells, were exclusively ipsilateral. The SNc projections were also more specific with 3 non-overlapping thalamic injections backfilling only 27% of SNc cells compared to nearly 100% or more of PPN cells and 65% of LC cells. These findings implicate the thalamus as a novel site for disease specific alteration in DA neurotransmission; such as nigral degeneration attending Parkinson's disease. This was confirmed in hemiparkinsonian rats and monkeys where reduction of thalamic DA innervation occurred coincident with signs of active axonal degeneration. Individual mesencephalic DA neurons therefore have the potential to modulate normal and pathological behavior not only through traditional nigrostriatal pathways, but also via axon collaterals innervating the thalamus. These pathways likely modulate thalamocortical arousal state given the diffuse thalamocortical dysrhythmia, impairments of wakefulness and REM-sleep, and reduced cell firing in motor thalamic nuclei in PD.

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## DECREASED TONIC AND PHASIC ACTIVITY DURING REM SLEEP IN UNTREATED PARKINSON'S DISEASE

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Impairment of movement with akinesia, rigidity and tremor are cardinal features of Parkinson's disease. REM Sleep Behavior Disorder (RBD), a disorder characterized by excessive muscle twitching and lack of atonia with injurious behavior during REM Sleep, is frequently associated to, and may precede the onset of Parkinsonism. When associated, both disorders may share motor dyscontrol during REM sleep. **OBJECTIVE:** The objective of this study was: a) to assess whether motor dyscontrol during sleep precedes the onset of daytime symptoms in Parkinson's Disease (PD), and b) to investigate the effect of l-dopa treatment on motor activity during REM sleep in PD patients. **METHODS:** 14 consecutive, recently diagnosed and treatment-naïve PD patients (5 females, 9 males) suffering idiopathic Parkinson's disease underwent all-night polysomnographic (PSG) studies. Sleep studies were repeated following a mean 184 treatment period with a low dosage of l-dopa (mean dosage: 360 mg). Age (mean: 75.3 years) and gender-matched healthy subjects were used as controls. A sleep study was repeated on 4 patients following withdrawal of treatment for 1 week.

PSG- studies were recorded and scored according to standard methods. The tonic and phasic components of REM sleep were scored separately, according to the criteria used by Lapierre and Montplaisir (1992):

1. Tonic motor activity: Each 20 second-epoch was scored as "tonic" or "atonic" depending on whether tonic chin EMG activity was present for >50% or <50% of the epoch.
2. Phasic motor activity was quantified as:
  - a. EMG twitches: The % of 2 seconds epochs containing phasic EMG twitches. The latter were defined as any burst of EMG activity lasting 0.1 to 5 seconds with an amplitude exceeding 4 times the background EMG activity.
  - b. REM density: The number of Rapid Eye Movements (REMs) per minute of REM-sleep.

Data were analyzed by means of non-parametric statistics (Wilcoxon and Mann-Whitney tests). **RESULTS:** No differences were observed between the groups or conditions regarding sleep architecture, PLM(periodic leg movements)-index or apnea-hypopnea-index. Compared to controls, untreated PD patients showed a reduction in phasic twitching activity ( $2.1 \pm 2.5$  vs  $5.4 \pm 4.6$ ;  $p < 0.05$ ). Following treatment with l-dopa, a statistically significant increase in both tonic motor activity (495%;  $p > 0.05$ ) and phasic twitching (280%;  $p < 0.01$ ) could be observed. No differences were observed between treated PD patients and controls. Furthermore, withdrawal of l-dopa treatment led to a reduction of phasic chin EMG activity to pre-treatment values (n.s.). **CONCLUSIONS:** Phasic and motor activity during REM sleep was reduced in untreated Parkinson's disease as compared to controls. Treatment with l-dopa not only improved daytime symptoms but increased both phasic and tonic motor activity during REM sleep. The l-dopa induced increase in phasic and tonic motor activity during REM-sleep approached the degree of activity observed in controls. Short term discontinuation of l-dopa treatment in 4 patients resulted in a return to baseline (pre-treatment) values of phasic but not of tonic activity. Taken together, the results suggest that the reduction of phasic activity in de novo PD patients improves as a result of treatment. In contrast, the increase over time in tonic activity takes place as a result of the progression of illness, rather than as a result of treatment.

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## EEG SPECTRAL ANALYSIS BEFORE AND AFTER SLEEP IN HIGH-FUNCTIONING AUTISM

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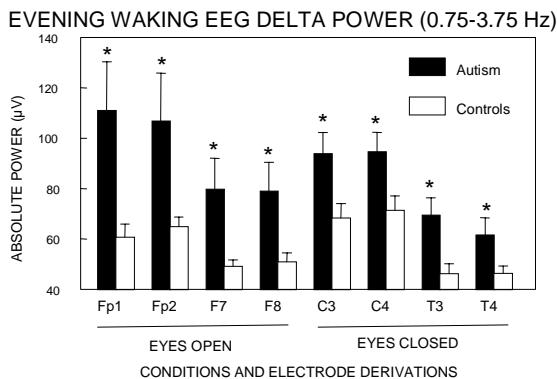
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Studies report evidence of frontal and temporal lobe dysfunction in autism (1). We verified whether these atypicalities could be put to evidence during waking EEG and if results would be sensitive to the effect of nocturnal sleep.

**Method:** Seven participants with autism (Group A, 7M; age: 22.1 ± 14.5) with normal IQ were compared to seven healthy controls (Group C, 7M; age: 25.7 ± 14.0). Waking EEG was recorded from four cerebral regions: Frontal (FP, FP, F, F), Central (C, C), Temporal (T, T), and Occipital (O, O) before and after the night using a monopolar montage referred to linked ears. Subjects were recorded for five minutes with eyes closed (EC) and 5 minutes with eyes opened (EO) on each moment. Spectral analysis was performed on 10 to 15 four-second epochs on absolute power (mV/Hz, 0.75Hz to 19.75Hz). Four frequency bands were created: Delta (0.75-3.75 Hz), Theta (4-7.75 Hz), Alpha (8-12.75 Hz), and Beta (13-19.75 Hz). Groups were compared with t-tests.

**Results:** Before sleep, in the EC condition, Group A showed higher Delta power than controls for the Central and Temporal regions. In the EO condition, Group A showed higher Delta and Theta power in the Frontal region. After sleep, EEG power was no more different between groups in any condition.

**Discussion:** Participants with autism showed high spectral power values for slow-wave activity in Frontal, Central, and Temporal regions, a difference that disappeared after a night of sleep. These results suggest that: 1) evening fatigue levels are increased in autism compared to controls, following a day of sustained wakefulness; 2) sleep restorative functions are optimal in autism.



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A DOUBLE BLIND PLACEBO CONTROLLED TRIAL OF MODAFINIL IN  
PARKINSON'S DISEASE PATIENTS WITH EXCESSIVE DAYTIME  
SLEEPINESS

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The goal of this study was to assess the therapeutic efficacy of modafinil in the treatment of increased daytime sleepiness in Parkinson's disease (PD).

*Methods:* 12 patients with idiopathic Parkinson's disease (9 m, 3 f;  $65.0 \pm 7.6$  years, disease duration  $6.8 \pm 4.1$  years) and increased daytime sleepiness (Epworth sleepiness score ESS 10 or more) completed this double blind, placebo controlled, randomized, crossover study. Patients with daytime sleepiness due to otherwise treatable causes were excluded. In two two-week treatment blocks patients received placebo or 200 mg modafinil (100 mg during the first treatment week) as a single morning dose in a randomized crossover order. Antiparkinsonian treatment was kept unchanged for the duration of the study. At baseline and at the end of each treatment block sleepiness was evaluated using subjective (ESS) and objective measures (maintenance of wakefulness test MWT, a variation of the MSLT).

*Results:* Epworth sleepiness scores were significantly improved with modafinil (mean score improvement  $3.42 \pm 3.90$ ) compared to placebo ( $0.83 \pm 1.99$ ;  $p = 0.011$ , paired t-tests). Sleep latency in the MWT was marginally improved; before / after placebo 10.7 (2.2-40) / 12.4 (25-40) minutes and before / after modafinil 10.5 (0.8-40) / 16.8 (4.2-40) minutes ( $p < 0.1$ ).

*Conclusion:* The results of this study suggest, that modafinil is an effective treatment for daytime sleepiness in PD patients.

SCREENING OF SLEEP AND CIRCADIAN RHYTHMS IN MAJOR  
DEPRESSION: SLEEP AND WAKE COMPLAINTS (Part 1)

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The questionnaire was aimed at identifying different profiles of depressed patients before treatment on the basis of sleep complaints, circadian typology and daily course of depressive symptoms.

The questionnaire included nine items. Sleep and wake complaints were evaluated by the first five items: 1. difficulties falling asleep; 2. repeated night-time awakenings; 3. early morning awakenings; 4 difficulties being wide awake after awakening; and 5. sleepiness during the day.

The questionnaire was administered to 574 patients with a major depressive episode (DSM-IV criteria), single or recurrent (HDRS score  $\geq$  22). 92% completed correctly the questionnaire.

Patient mean age was  $44.5 \pm 12.5$  years, there were 413 women and 161 men. The mean HDRS score was  $26.5 \pm 4.0$ .

58% experienced difficulties falling asleep, 60% experienced repeated night-time awakenings, 52% experienced early morning awakenings, 36% complained of difficulties being wide awake after awakening, and 38% experienced daytime sleepiness.

A principal component analysis revealed two clear cut dimensions (see figure), one related to insomnia (the first three items) and the other related to daytime sleepiness (the two last items). These two dimensions did not correlate ( $r = 0.019$ ).

These results study are in agreement with those of other studies using different methodologies. More patients experienced symptoms of insomnia than daytime sleepiness.

HYPERSOMNIA IN SUPRATENTORIAL BRAIN TUMORS: A SYMPTOM  
FREQUENTLY NEGLECTED  
RESULTS OF A 24 HOURS POLYGRAPHIC RECORDING

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Several clinical reports have denoted the existence of hypersomnia in thalamic and brain stem tumors, according with the presence of sleep centers in those anatomical locations.

Concurrently, few communications report the presence of the same symptom in supratentorial brain tumors.

*INTRODUCTION:* A 38 years old female, with no pathologic previous clinical history, and without previous sleep disorders, began suddenly with hypersomnia. She slept almost all days during three months, waking up only to eat or void 2 or 3 times a day. Besides the hypersomnia, general physical examination and clinical neurological explorations were totally normal. She took no medications and there was no history of drug abuse.

A psychiatric origin of her hypersomnolence was first suspected, and her doctor treated her with antidepressants during 2 months, without satisfactory clinical response. She was then sent to Hospital to perform further studies, as the extended sleep continued.

*MATERIAL AND METHODS:* A polygraphic recording of 24 hours was performed at her admittance to Hospital. A Computerized Tomography performed immediately after hospitalization, showed a pathological image on the superior parasagittal surface of left parietal lobe corresponding to a solid tumor of 7 cm width, which had important anatomical relationship with the venous sinus and the falx and which was homogeneously contrast-enhanced with Gadolinium.

*RESULTS:* The polygraphic all-day recording prior to the surgical exeresis of the tumor, during which she slept 70% of the time, showed increased amount of slow wave sleep, specially stages I and II. Nocturnal sleep was slightly disrupted, because of "first night effect" and because she had to be awakened in order to be treated with intravenous corticoids.

Pathological exams of the tumor showed that it was a meningioma with no further malignant cells. 48 hours after surgical exeresis, hypersomnia had completely receded, and she regained the normal amount of sleep and circadian rithmicity she had before. Evolution was excellent further on.

*DISCUSSION:* Hypersomnia is frequently misdiagnosed and neglected as clinical neurological symptom which may indicate the presence of organic brain disease, specially in young otherwise healthy subjects. In this case, as the venous sinus was involved, pathological edema and flow disturbances could have affected infratentorial sleep structures, thus producing the hypersomnia.

## NIGHT SLEEP OF PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

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Amyotrophic lateral sclerosis (ALS) is progressive disease characterised by the reduction of central and peripheral motor neurons. The respiration insufficiency is its major and fatal complication occurring within a few months after the first appearance of the symptoms. The respiratory insufficiency is usually more prominent during sleep. The aims of the study were to evaluate the quality of the sleep in subjects suffering from ALS, to evaluate the degree of sleep respiratory disturbance in patients having no signs of respiratory insufficiency by day and finally to select the patients for ventilation support by positive intermittent ventilation.

In total 9 subjects were examined: 6 men, 3 women; average age 60.1 (SD=6.9) years, BMI 25.8 (4.3). Norris's score was 71.4 (11.2) and the average duration of the disease was 1.8 (0.5) years. 5 of them were treated by riluzol. EEG, EOG, EMG of mental and tibialis anterior muscles, ECG, respiratory flow in front of the nose and the mouth, the chest and the abdomen movements, oxygen haemoglobin saturation, the body position and video were registered one night in a separate room by the on-line polysomnography system (Schwarzer Brain Lab). The records were analysed according standard rules (Rechtschaffen and Kales).

The sleep efficiency was 65.5 (8.9)% and the sleep latency 26,1 (24,6) min. The average proportions of sleep stages and wakefulness were following: 3+4 NREM sleep 11.2 (6.2) %, REM sleep 12.0 (4.4) %, wake after sleep onset 25.5 (8.7) %. The average AHI was 9.6 (7.8), but the AHI in REM sleep was 16.4 (21.5).

Records of 8 subjects showed a completely abnormal sleep structure without normal NREM/REM cycles, with the reduction of 3+4 NREM sleep and the reduction of REM sleep. In 4 subjects important number of apnoeas and hypopneas were found during REM sleep. Nobody was recommended to ventilation support during the night. Periodic leg movements in sleep (PLMS) were found in 4 patients. Respiratory problems and namely PLMS were partly reasons of sleep abnormality.

*Summary:* The sleep of ALS subjects was disturbed. Respiratory disturbances and PLMS did not explain this sleep abnormality completely.

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## SLEEP DISTURBANCES AND DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Introduction.** This study describes the polysomnographic sleep changes associated with Lupus disease activity and their relationship with depression and level of fatigue.

**Methods.** Twenty four Systemic Lupus Erythematosus (SLE) female patients, mean age of  $36.7 \pm 11.3$  years with a mean body mass index (BMI) of  $25.5 \pm 3.9$  kg/m<sup>2</sup> agreed to participate in the study. All fulfilled at least 4 of the American College of Rheumatology revised criteria for SLE. Disease onset occurred  $11.1 \pm 8.7$  years prior to the study. Disease activity was scored according to the SLE Disease Activity Index (SLE-DAI), which was adapted for and validated in a Mexican population (MEX-SLEDAI). Eleven patients were receiving corticosteroids plus immunosuppressants (mean dosage of prednisone 5.3 mg/day, azathioprine 50 mg/day), 3 were receiving antimalarials (chloroquine 275 mg/day), 3 were receiving steroids plus immunosuppressants plus antimalarial drugs (prednisone 10 mg/day, azathioprine 100 mg/day, and chloroquine 240 mg/day). Patients were classified into two groups according to the disease activity score: Active-SLE-Group  $\geq 2$ , Non-Active-SLE-Group  $< 2$ . The patients underwent all-night polysomnography on 2 consecutive nights. They also completed the Beck Depression Inventory and the Fatigue Severity Scale (FSS).

**Results.** The polysomnographic data showed that Active-SLE-Group had more light sleep (Stage 1% =  $13.2 \pm 3.7$ ) than Non-Active-SLE-Group (Stage 1% =  $9.2 \pm 3.6$ ),  $t=2.6$ ,  $p<0.02$ ; increased number of sleep stage transitions (Active-SLE-Group =  $168.4 \pm 27.8$  versus Non-Active-SLE-Group =  $137.7 \pm 33.44$ ,  $t=2.5$ ,  $p<0.03$ ); and less delta sleep % (Active-SLE-Group =  $10.9 \pm 4$  versus Non-Active-SLE-Group =  $15.8 \pm 6.1$ ,  $t=2.4$ ,  $p<0.03$ ) and they also reported a higher level of fatigue (FSS =  $4.7 \pm 1.7$ ) than Non-Active-SLE-Group (FSS =  $3.0 \pm 2.0$ ),  $t=2.4$ ,  $p<0.03$ ; but about the same level of depression (Active-SLE-Group =  $17.5 \pm 9.1$  versus Non-Active-SLE-Group =  $12.1 \pm 8.3$ ,  $t=1.6$ ,  $p<0.13$ ). MEX-SLEDAI score correlated with fatigue level (Spearman  $\rho=0.41$ ,  $p<0.04$ ), sleep Stage 1% ( $\rho=0.46$ ,  $p<0.03$ ) and number of sleep stage transitions ( $\rho=0.54$ ,  $p<0.007$ ).

**Conclusion.** These preliminary results suggest that Lupus disease activity has an impact on sleep quality and on the level of fatigue but it is not related with the depression level.

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## FREQUENCY OF SLEEP DISORDERS IN PATIENTS WITH EPILEPSY

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**METHODS AND PATIENTS:** Fifty (n=50) consecutive patients (27 men, 23 women, aged 19-69 years, mean 47 years) admitted in a specialized outpatient clinic, completed a questionnaire with 108 standardized questions concerning sleep-wake habits and symptoms. Body mass index exceeded 25 in (n=15) and 30 in (n=5). Epilepsy was partial in 14 and generalized in the remaining 36 cases. Patients were treated with a mean of 1.8 antiepileptic medicaments (range 0-4). The epilepsy was considered as refractory to therapy in 12 patients. At least rare nocturnal seizures appeared also in 12 cases. **RESULTS:** Sleep-wake complains included sleep-onset and sleep-maintenance insomnia (n=30), restless-legs symptoms (n=26), parasomnia (n=20), hypersomnia defined as a epworth sleepiness score >10 (n=10) and fatigue (n=29). Habitual snoring (always or almost always) was present (n=27), and sleep-apnoe considered probable by questionnaire (SA-SDQ>32 for women and SDQ>36 for men) (n=10). Dreams were recalled at least sometimes (n=33) or every night (n=10). **CONCLUSION:** This preliminary results of a ongoing project suggest a high prevalence of sleep-wake complaints in a unselected population of patients with epilepsy. Their relevance of this findings for seizure activity and control remains to be assessed.