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CENTER FOR SLEEP STUDIES

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Sleep laboratory: polysomnography recording

The Center for Sleep Studies is based at Federal University of São Paulo (Unifesp).

While the primary function of sleep remains unknown, the fact that prolonged sleep deprivation (SD) leads to death in humans and experimental animals indicates that sleep is essential for survival (*Perspect. Biol. Med*., **41(3)**:359-90, 1998). The biological significance of sleep is further signaled by the fact that it occurs in most species despite being apparently maladaptative with respect to other biological properties such as feeding, avoiding predators, and reproducing. Most organisms literally "fall asleep" as a normal behavior, and will experience an increasingly strong urge to do so if deprived of sleep. That the consequences of this overpowering urge to sleep may be disastrous in a number of situations is exemplified in accidents involving motor vehicles or heavy machinery.

The causes, mechanisms and consequences of SD and the physiological basis of the resulting need for sleep constitute the central focus of the research work proposed by our RIDC Center. Our goals are to expand scientific understanding of sleep functions by addressing the broad spectrum of consequences of sleep loss, and to develop and validate new diagnostic and therapeutic approaches to sleep-related conditions.

MAIN RESEARCH TOPICS

Effects of sleep deprivation on dopaminergic neurotransmission

Sleep and cognition

Circadian rhythms

Sleep, genital reflexes and hormones

Autoimmune diseases and sleep disorders

Sleep fragmentation and chronic pain

Breathing disorders related to sleep, with an emphasis on obstructive sleep apnea syndrome

Cardiovascular and metabolic alterations in sleep disorders

Relationship between physical activity and sleep

Sleep, somnolence, fatigue and accidents

Movement disorders during sleep

Cytotoxic effects of sleep deprivation

Sleep disorders resulting from malformations

Molecular and genetic mechanisms in sleep

Epidemiological genetics and phenotypes in sleep

SUMMARY OF RESULTS TO DATE AND PERSPECTIVES

The apnea-hypopnoea index is not enough to diagnose obstructive sleep apnea
There is a great individual variability in the stability of the apnea-hypopnoea index (AHI) from one night to another. Thus, for an adequate obstructive sleep apnea diagnosis, AHI should be used along with other clinical and polysomnographic parameters.

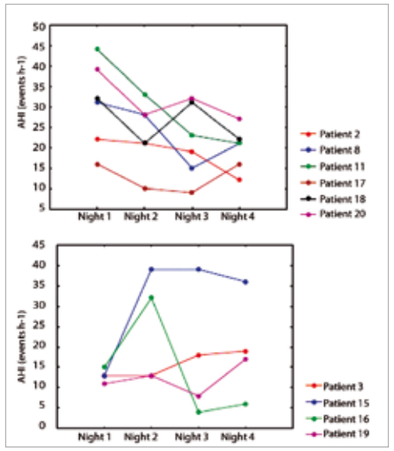

Figure 1: *Apnea-hypopnoea index (AHI) in the outpatients (50%) who had variable measures, and therefore would receive different obstructive sleep apnea diagnosis, during four consecutive nights (J.* Sleep Res. ***10****:245-51, 2001)*

Development of an animal model of Periodic Leg Movement (PLM)
Considering our observation that paraplegic individuals present frequent periodic leg movement (PLM), we proposed an animal model of PLM based on the higher incidence of limb movements during non-REM sleep in spinal cord injured (SCI) rats. Our model demonstrated that these movements may be generated in the spinal medulla without involvement of cortical structures (*Brain Res.* **1017**:32-8, 2004).

Mechanisms of paradoxical sleep deprivation-induced amnesia
We have demonstrated the involvement of oxidative stress in the amnesic effect of paradoxical sleep deprivation (PSD) in mice (*Neuropharmacology*, **46**:895-903, 2004), the anti-amnestic effect of antioxidant agents (*Neuropharmacology*, **46**:895-903, 2004) and the pro-amnesic effect of pro-oxidants (*Prog. Neuropsychopharmacol. Biol. Psychiatry*. **31**:65-70, 2007) in mice submitted to PSD. In addition, we have demonstrated that the amnesic effect of PSD in mice is also related to a concomitant anxiogenic effect of PSD (*Neurobiol. Learn. Mem*. **82**:90-8, 2004), is not related to modifications in GABAergic transmission, but is mediated by noradrenergic transmission (*Psychopharmacology*. **176**:115-22, 2004).

Mechanisms of sleep deprivation-induced facilitation of genital reflexes
The facilitatory effect of paradoxical sleep deprivation (PSD) on spontanelously genital reflexes in rats is associated with increased concentrations of progesterone and is dramatically potentiated by cocaine administration (*J. Neuroendocrinol*. **16**:154-9, 2004).

Anestrus in paradoxical sleep deprived female
Sleep deprivation presents distinct, long-lasting effects on estrous cycle (leading to a prolonged period of anestrus), and may modulate the ovarian hormone release through alterations in hormonal-neurochemical mechanisms (*Horm. Behav*. **49**:433-40, 2006).

The hyperfagia/weight loss paradox during sleep deprivation
The hyperfagia/weight loss paradox in sleep deprived rats results from difficulties in obtaining food to reach energetic needs especially during the first day of sleep deprivation, after which the animals adapt to the procedure (*Sleep*, **29**:1233-8, 2006).

A double-blind, placebo-controlled, crossover study of sildenafil in obstructive sleep apnea (OSA)
Sildenafil taken close to bedtime significantly worsens respiratory and oxygen saturation (SaO_2) variables during sleep in men, when compared to placebo.

Acupuncture is an effective treatment for moderate obstructive sleep apnea syndrome
Ten weekly sessions of acupuncture significantly improved the respiratory events of patients presenting with moderate OSAS in comparison to treatment with the sham procedure (needle insertion in non-acupoints) and to non-treated controls. Acupuncture also improved quality of life and decreased subjective sleepiness (*Sleep Med*. **8**:43-50, 2007).

Worsening of sleep complaints: an epidemiological study
We compared the prevalence of complaints of insomnia, excessive diurnal sleepiness, parasomnias, and sleep habits of the adult population in the city of São Paulo, Brazil, estimated in surveys carried out in 1987 and 1995 (1000 adult each; *Braz. J. Med. Biol. Res*. **40**:1505-15, 2007). Difficulty in maintaining sleep, initiating sleep and early morning awakening

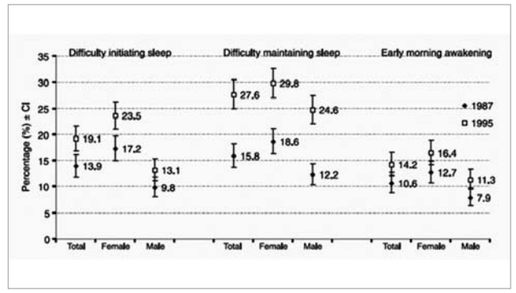

Figure 3: Insomnia complaints by gender in surveys carried out in 1987 and 1995 in the city of São Paulo (representative samples of 1000 adults per survey). Sleep complaints increased in 1995. Data are reported as percentages ± confidence interval (CI) at 95% (Z-test)

significantly increased throughout time, mainly in women. Besides sleeping slightly less, interviewees went to bed and woke up later in 1995. These major changes over a little less than a decade's time should be considered as an important public health issue.

Donepezil decreases apnea/hypopnoea in Alzheimer's patients
We found that donepezil improves apnea/hypopnoea index and oxygen saturation during sleep in Alzheimer disease patients with obstructive sleep apnea, despite REM sleep increase. This was the first controlled trial to show this magnitude of improvement of respiratory parameters, during sleep, with one drug (*Chest*. **133**:677–683, 2008).

Gene expression changes after sleep deprivation (unpublished data)
Paradoxical sleep deprivation promotes a number of behavioral, physiological, as well as cellular functioning alterations, including gene expression in specific brain regions. A total of 55 genes were found to be differently expressed in rats after 96 hours of sleep deprivation. Interestingly, after 24 hours of sleep recovery (rebound), approximately 50% (n=25) of the PSD genes had their expression returned to control levels. Also, 200 transcripts, such as Adenosine A2B receptor, Insulin receptor substrate2, Corticotropin releasing hormone, and Homer1, were specifically altered when compared to sleep deprivation condition. These data raise a number of potential candidates for the molecular basis of homeostatic mechanism of sleep regulation.