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Editorial

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On sleepy humans and sleepy rats

In view of the present day practice of sleep medicine, it is rather surprising that until the mid-1970s, scientific literature dealing with sleep disorders in the general population hardly touched on the complaint of excessive sleepiness. This, however, does not mean that sleepy patients were completely absent from the medical literature. In Dickens's *Pickwick Papers*, Joe, the boy servant who impressed Mr Pickwick by his constant tendency to fall asleep, inspired several physicians to coin the phrase 'Pickwickian' to denote sleepy patients. In the 21st century, sleepiness has become a major clinical and research subject. Suffice to mention that Murray John's paper describing the Epworth Sleepiness Scale (ESS), the popular subjective self-completed questionnaire to assess sleepiness, is the second most cited paper among all sleep-related publications (Johns, 1991). The 2008 December issue of *Journal of Sleep Research* includes a collection of papers addressing the subject of 'sleepiness' from several interesting angles such as how to measure sleepiness objectively in an animal model? what are the determinants of sleepiness in sleep apnoea patients? is it possible to differentiate between the overlapping complaints of fatigue and sleepiness in patients with chronic fatigue syndrome? what are the consequences of sleep debt on daytime sleepiness? and what are the effective countermeasures of sleepiness?

There is a great number of methodologies to measure sleepiness objectively in humans. The most widely used are the multiple sleep latency test (MSLT) in which sleepiness is operationally defined as the propensity to fall asleep during 4–5 planned naps during the day, and the psychomotor vigilance test (PVT) that measures sleepiness by performance impairment (Carskadon *et al*., 1986; Jewett *et al*., 1999). So far, validated techniques to measure sleepiness in animals are sparse. The first two papers in the this issue of JSR by McKenna *et al*. 'Assessing sleepiness in the rat: a multiple sleep latencies test compared to polysomonographic measures of sleepiness', and by Christie *et al*. '24 hours of sleep deprivation in the rat increases sleepiness and decreases vigilance: introduction of the rat-psychomotor vigilance test', both from the same research group from Harvard Medical School, provide animal versions of the MSLT and PVT analogous to the human tests. The rat MSLT requires only 3 h of testing and, similar to the human version, produces a minimal amount of additional sleep loss associated with the procedure itself. McKenna *et al*. showed that 6 h of sleep deprivation significantly shortened the rat MSLT latencies regardless of circadian and illumination influences, and that it was as sensitive a measure as conventional polysomnographic indirect measures of sleepiness. Christie *et al*. developed a rat PVT that closely resembles the human version. In an operant conditioning paradigm, rats are required to monitor a central stimulus location (light) for a brief and unpredictable signal (flash of light) to which they respond with simple intrinsic behaviour (a nose-poke) rewarded with water. Rats experiencing 24-h sleep deprivation just prior to performing the rat PVT demonstrated behavioural impairment analogous to that of sleep-deprived humans – i.e. response latencies slowed and lapses increased. Both the rat MSLT and PVT will allow investigation of the neurobiological mechanisms underlying sleepiness in the rat model.

Although clinical experience shows that sleepiness is the cardinal symptom of sleep-disordered breathing, Koutsourelakis *et al*. convincingly demonstrate that the origin of sleepiness in patients with sleep apnoea syndrome is multifactorial, and that sleep apnoea severity is only one of three independent factors that contribute to sleepiness. In their paper 'Determinants of subjective sleepiness in suspected obstructive sleep apnoea', they report that the severity of sleep apnoea, depression and diabetes, contributed the lion share of the variance in the ESS score, used to measure subjective sleepiness. Interestingly, polysomnographically determined sleep measures were not independently related to sleepiness. Thus, the results of Koutsourelakis *et al*. should warn sleep clinicians from assuming that the apnoeas and sleep fragmentation are the sole causes of excessive daytime sleepiness in sleep apnoea syndrome. Neu *et al*., in their paper 'Are patients with chronic fatigue syndrome just 'tired' or also 'sleepy'?' addressed the interesting question of the possible overlapping between complaints of 'fatigue' and 'sleepiness'. Using the MSLT to measure daytime sleepiness in two groups of patients with chronic fatigue syndrome and sleep apnoea syndrome, and in healthy controls, they report that chronic fatigue patients, free of any other medical or psychiatric co-morbidities, showed normal sleep latencies in spite of their subjective complaints of fatigue and sleepiness that were significantly higher than in healthy controls, and no different from patients with sleep apnoea. Noteworthy, although patients with chronic fatigue could not be considered objectively sleepy, their sleep latencies were significantly shorter than in the control group.

The question how to counteract mid-afternoon and evening sleepiness is the subject of Horne, Anderson and Platten's paper: 'Sleep extension versus nap or coffee, within the context of ''sleep debt.'' They compared the effects of three counter-

measures: extending night sleep up to 90 min beyond the normal wake-up time, a 20-min nap within a 30-min period starting at 14:30 h, and 150 mg caffeine consumed at 14:00 h, on mid-afternoon–evening sleepiness levels measured by MSLT and subjective scales. While sleep extension improved MSLTs by approximately 1–2 min, this improvement was no better than caffeine and was exceeded to a significant degree by the short nap. Within the context of the ongoing controversy on the effects of sleep debt in modern societies, Horne *et al.* concluded that a modest amount of afternoon sleepiness is not indicative of a lack of night-time sleep, but should be seen as within the bounds of normality reflecting an endogenous harmonic of the circadian system. 'Sleep debt' and its consequences is also the subject of Meijr's paper: 'Chronic sleep reduction, functioning at school and school achievement in preadolescents'. Meijr investigated 436 children aged 9–14 years in 12 elementary schools in the Netherlands by a questionnaire specifically designed to investigate chronic sleep reduction, a 2-week sleep log, and questionnaires concerning functioning at school and school achievements. Using structural equation modelling, she found that the chronic sleep-reduction questionnaire designed specifically for this study reflected more sleep quality rather than sleep duration, and that chronic sleep reduction significantly contributed to self-reported school achievement. Interestingly, these results were stronger for girls than boys.

Son *et al.*'s paper on the 12-h shift system in the automobile factories in Korea deals with sleepiness in shift workers. They report that night shift workers who worked for 12 h or more a day were exposed to the risk of severe sleepiness. Alarmingly, two-thirds of the workers worked 6–7 consecutive days per week, totalling 66–85.5 h of work. Not surprisingly, 61.2% of the night shift workers were suffering from severe sleepiness at the end of their shift in comparison with 9.5% of the day workers. The authors call for immediate measures to address these work patterns in the Korean automobile industry.

Can we draw any general conclusions from this collection of papers? Personally, I perceive a clear message emerging: sleepiness that on many occasions is seen within the narrow context of sleep disorders is a multifactorial phenomenon. It may be influenced and modified by a wide range of factors beyond sleep disorders such as disease states, mental states, extended working hours and sleep debt. These interact with the circadian clock to produce the powerful sensation of closing eyelids and surrender to sleep.

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