British Neuropsychiatry Association AGM and joint conference with the Section of Neuropsychiatry of RCPsych, 9–11 February 2011, Institute of Child Health, Central London

Oral presentations

**OP.01 THE NEUROBIOLOGY OF SLEEP**

E Szabadi.

**Elemer Szabadi** is Professor Emeritus of Psychiatry and Consultant Psychiatrist at the University of Nottingham. His clinical qualifications are MD (Budapest), DipNeurol (Budapest), FRCPsych (London), and his research qualifications are PhD (Edinburgh), DSc (Manchester). He was trained in Medicine at Semmelweis University Medical School in Budapest, where he obtained a post-graduate qualification in Neurology. In 1969, he moved to Edinburgh where he was engaged in full-time laboratory research in electrophysiology for 6 years. In 1974, he became a member of the Royal College of Psychiatrists. In 1975, he moved to Manchester where he held academic appointments in Clinical Psychiatry until 1990, when he was appointed Professor of Psychiatry and Head of Department at the University of Nottingham. In 2004, he retired from his University appointment, but continued in full-time research as Professor Emeritus. He is also continuing to provide a clinical assessment service in Neuropsychiatry. His current research interests are in the field of psychopharmacology (sleep/arousal mechanisms and autonomic regulation in humans, neurobiology of timing in experimental animals).

It has been established in the course of the past decade that the level of arousal at any time reflects an intricate interplay between a number of distinct wakefulness-promoting and sleep-promoting nuclei located in the hypothalamus/thalamus and brainstem. All these nuclei are associated with distinct neurotransmitters. Wakefulness-promoting nuclei include the tuberomamillary nucleus (histamine) and the lateral hypothalamic/perifornical area (orexin) of the hypothalamus, the intralaminar neurones of the thalamus (glutamate), and a number of monoaminergic nuclei in the brainstem (raphé nuclei: serotonin, locus coeruleus: noradrenaline, ventral tegmental area of mid-brain: dopamine), and the pedunculo-pontine tegmental nucleus (PPT: acetylcholine). The major sleep-promoting nucleus is the ventrolateral preoptic nucleus of the hypothalamus (VLPO) utilising GABA. During wakefulness the wakefulness-promoting nuclei are active, whereas the VLPO is quiescent, and the reverse pattern operates during sleep. While the VLPO is active during slow-wave sleep, rapid eye movement sleep is associated with the activation of some cholinergic neurones in the PPT. The alternation between states of wakefulness and sleep shows a circadian pattern, which is regulated by the “internal clock” of the hypothalamus (suprachiasmatic nucleus (SCN)). Light has a profound effect on the sleep/wakefulness cycle by aligning it to the night/day cycle (“photoentrainment”). Light also has a direct acute effect on the level of arousal, being sleep-promoting in nocturnal animals and wakefulness-promoting in diurnal animals. The effect of light on the level of arousal is mediated by the recently discovered intrinsically photosensitive ganglion cells of the retina, which operate via the photopigment melatonin. These ganglion cells give rise to the retina-hypothalamic tract, which projects to the VLPO and the SCN. The SCN, on the other hand, sends excitatory projections to some wakefulness-promoting nuclei (locus coeruleus, orexin neurones of the lateral hypothalamus). In both nocturnal and diurnal animals the stimulation of the VLPO via light has a sleep-promoting effect, which, however, is likely to be superseded by the wakefulness-promoting effect of the stimulation of the SCN in diurnal animals. Light exerts an additional alerting effect by inhibiting the synthesis of the sleep-promoting hormone melatonin. Drugs can modify the activity of the sleep/arousal network by interacting with either sleep-promoting or wakefulness-promoting neurones. Agonists of the sleep-promoting system reduce and antagonists increase the level of arousal, whereas agonists of the wakefulness-promoting system increase and antagonists decrease the level of arousal. Thus, for example, drugs used for the treatment of insomnia are either agonists of the GABA-containing sleep promoting system, or antagonists of the monoaminergic and orexinergic wakefulness-promoting arousal systems.

**OP.02 RESTLESS LEGS, PERIODIC LIMB MOVEMENTS AND BREATHING PROBLEMS**

A Williams.

**Adrian Williams** graduated from University College Hospital, London and, after training in General Medicine there, took up a lectureship at The Cardiothoracic Institute, Brompton Hospital, investigating the pulmonary changes associated with chronic liver disease. In 1975 Dr Williams was recruited to Harvard Medical School, Boston where his interest in sleep began with the investigation of Sudden Infant Death Syndrome (S.I.D.S.) and publication of a definitive study implicating obstructive sleep apnoea (OSA) as one cause of this syndrome.

An invitation to the University of California at Los Angeles in 1977 to take up a post as Chest Physician allowed this early interest in OSA in infants to extend into adult patients with the very first reports of OSA causing hypertension, and of oximetry as a natural diagnostic tool. In 1985 Dr Williams became tenured Professor of Medicine at UCLA and co-director of the UCLA Sleep Laboratory.

As Sleep Medicine gelled as a specialty, Dr Williams was one of the first to take the Board exams in 1989 to become an accredited polysomnographer and later member of the American Academy of Sleep Medicine.

In 1994 Dr Williams returned to London where he established the Sleep Disorders Centre at St. Thomas’ Hospital. He has published extensively on Sleep Disorders including more than 100 peer reviewed original scientific papers and more than 80 other published papers including chapters and books.

Dr Williams is a Diplomat of the American Board of Sleep Medicine, a founding member of The British Sleep Foundation, the Sleep Medicine Section of the Royal Society of Medicine as well as the RLS UK Group, and was recently appointed Professor of Sleep Medicine, King’s College London.

Sleep complaints are among the commonest in medical practice and can be simply categorised as:

- disturbances of getting to sleep or staying asleep, or unrefreshing sleep, that is insomnia,
- excessive daytime (or more properly wake-time) sleepiness, that is, hypersomnia; and
- things that disturb the individual’s sleep commonly said to be “things that go bump in the night”, or parasomnias.

Although insomnia and parasomnias are prevalent, the hypersomnias are considered more prominently because of the potential impact on the household and on society.
Abstracts

Conditions that will produce excessive wake-time sleepiness are also relatively few, specifically
- insufficient sleep,
- interrupted sleep such as might be caused by Restless Legs with Periodic Limb Movements or breathing problems, and
- intrinsic sleepiness or narcolepsy and its equivalents.

Restless Legs Syndrome (RLS) common with a general prevalence of 3–4%. It is a wakening complaint easily diagnosed by history (discomfort usually in the legs, occurring at rest, relieved by movement and confined mostly to the evening), associated 80% of the time with periodic limb movements in and disturbing sleep which might result in sleep complaints such as insomnia or hypersomnia. RLS may be secondary to renal failure and occurs in pregnancy and is promoted by anti-dopaminergics medicines such as the antihistamines. RLS is highly heritable and the genetic associations have recently been identified. The diagnosis of periodic limb movements in sleep usually requires polysomnography, although we have recently reported pulse rate variability on oximetry to be very useful. Treatment of both with a licensed dopa-agonist is common and second line treatment with codeine derivatives or clonazepam possible. Breathing problems are ubiquitous, the common form being snoring with obstructive sleep apnoea which affects some 5% of the population. The hallmark symptoms are snoring, witnessed apnoeas and excessive sleepiness with resulting sleep related vehicle accidents. Medical consequences include cardiovascular disease particularly hypertension, atrial fibrillation, stroke, along with neurocognitive abnormalities such as poor concentration, depression. Diagnosis is by history supplemented by a sleep study, often oximetry. When associated with symptoms such as sleepiness treatment with continuous positive airway pressure is usually advised along with weight loss in the obese. An alternative therapy would be an oral appliance for mandibular advancement. Both are successful mechanical treatments aimed at making the collapsing pharyngeal airway more patent. Surgery is rarely used.

S Eriksson.

Dr Sofia Eriksson started her medical career in Sweden before moving to London to join the Department of Clinical and Experimental Epilepsy at the Institute of Neurology. She is now working as a consultant neurologist at the National Hospital for Neurology and Neurosurgery in London, specialising in epilepsy and neurological sleep disorders.

Narcolepsy is a disorder of the relationship between sleep and wakefulness. This particularly affects REM sleep where features of REM sleep intrude into wakefulness and non-REM sleep. The cardinal symptoms are excessive daytime somnolence, cataplexy, hypnogogic hallucinations and sleep paralysis. Diagnosis is made using polysomnography and multiple sleep latency test showing short sleep latency and sleep onset REM. Narcolepsy with cataplexy is caused by loss of hypocretin producing neurons in the hypothalamus, possibly via autoimmune mechanisms. Stimulants such as Modafinil or Amphetamine derivatives are used to treat excessive daytime somnolence. Although Sodium Oxybate has been shown to effectively treat cataplexy, anti-depressants remain first line treatment in the UK.

Parasomnias are abnormal events occurring in association with sleep that are classified according to the sleep stage from which they occur. Some clinical features, such as timing of events during sleep, frequency of events and lifetime duration, are often helpful for the differential diagnosis of parasomnias.

Sleep-wake transition disorders occur during the transition between wakefulness and sleep and include rhythmic movement disorders such as head banging or body rocking, often seen in children. Episodes usually take place several times every night and may continue into adulthood. There have been discussions if these movements are a learnt behaviour and it is often difficult to treat.

Non-REM parasomnias occur from non-REM sleep, usually deep sleep and include sleep walking, sleep talking, confusional arousals and night terrors. Frequency of events varies but episodes occur most commonly in the first part of the night. Non-REM parasomnias are very common in childhood but may continue into adulthood. Safety aspects are the most important treatments to avoid injury to patient or bed-partner. Precipitants include sleep deprivation and stress. In more severe cases, medication such as long-acting Benzodiazepines or anti-depressant can be used. Non-REM parasomnias may be difficult to differentiate from nocturnal epilepsy.

REM sleep behavioural disorders (RBD) occur from REM sleep, often in the second half of the night. Onset is often after 50 years of age and there is an association with neurodegenerative disorders. RBD is characterised by loss of normal REM atonia associated with motor activity and sometimes dream enactment. RBD may be precipitated by anti-depressant medication and discontinuing medication will stop the events. Idiopathic forms are treated with long-acting Benzodiazepines or more rarely Melatonin.

It is sometimes possible to differentiate parasomnias on history alone, but often polysomnography is needed to clarify the diagnosis.

Katharina Wulff, PhD is currently a senior research scientist in Sleep and Circadian Neuroscience of the Nuffield Laboratory of Ophthalmology (NLO) at the University of Oxford. She studied biology in Berlin, Germany, and completed her PhD in chronobiology, studying the interactions between the well-established sleep-wake behaviour of parents and that of their developing newborn infants. The award of a EU Marie Curie Individual Fellowship allowed her to join the lab of Prof. Foster at Imperial College London in 2002, with whom she established new collaboration between his circadian molecular-focussed lab and labs with expertise in human sleep and psychiatry, linking basic circadian science with basic and clinical human research. Since then the lab moved to Oxford in 2007 where she is now leading the human chronobiology/sleep lab of the NLO.

Circadian rhythms are daily cycles in physiology and behaviour that are driven by an endogenous oscillator with a period of approximately (circa) one day (diem). The suprachiasmatic nuclei (SCN) of the hypothalamus constitute the master-oscillator coordinating circadian rhythms in the brain and periphery and simultaneously adjusting its neuronal activity to the environmental light-dark cycle. When subjects are isolated from environmental time cues such as social interaction and the light-dark cycle the oscillator still continues to define “day-time” activity and “night-time” inactivity and circadian rhythms are expressed, albeit with a longer than 24-h period (free-run) in humans. The circadian oscillator anticipates time-of-day, thereby enabling our complex physiology to prepare to the contrasting demands by giving catabolic
OP.02 Restless legs, periodic limb movements and breathing problems

A Williams

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