

# The Neurological Sleep Clinic – Part 1

## The Sleepy Patient

Traditionally, at least in the UK, sleep disorders have received a low profile in neurology training programmes such that only a handful of practising neurologists have an active interest in sleep medicine. As a consequence, most sleep centres are run exclusively by respiratory physicians who understandably focus, to varying degrees, on sleep-related breathing disorders. However, perhaps due to the astonishing developments in the neurobiology of primary sleep disorders, their inherent interest, together with an increasing recognition that abnormal sleep contributes to numerous common neurological conditions such as migraine and epilepsy, the situation is slowly changing. I have held a weekly 'Sleep Clinic' for seven years in the North-East of England and propose to summarise my personal approach to the assessment of sleep-related symptoms from a neurological perspective. It is often wrongly assumed that most patients with abnormal sleep require elaborate and expensive investigations in a "sleep laboratory". In fact, the reverse is true: if the diagnosis is totally unclear despite an accurate history, it is relatively rare for overnight investigations to illuminate the situation. I am particularly fond of an adage from a respected, now retired, doyen of sleep medicine, Professor David Parkes, namely: "A good sleep centre has far more need of a psychiatrist than an EEG machine".

In this, the first of a two part article, the assessment of sleepy patients will be discussed.

### Excessive daytime sleepiness

It is only fairly recently that the symptom of excessive sleepiness has been taken seriously by medical practitioners rather than being seen as a moral failing or sin. In a neurological sleep clinic, it is probably the commonest problem that prompts referral, usually with the implicit underlying question: "Is it narcolepsy?" Narcolepsy is almost certainly massively underdiagnosed, especially if the quoted prevalence rate of 0.05% is accepted. This is partly because there is clearly a spectrum of disease severity. This should not be too surprising given the underlying specific neurochemical deficiency in typical cases. In particular, most narcoleptics lose around 40,000 hypothalamic neurons containing the neuropeptide, hypocretin (or orexin) in adolescence, presumably by an autoimmune process. Although yet to be confirmed, it is entirely possible that a partial deficiency produces less severe or atypical forms of the syndrome that may be more difficult to recognise.

A detailed sleep-wake history, together with a number of directed questions, will usually allow a confident clinical diagnosis. It is important to recognise that the key element of narcolepsy is an inability to maintain stable states of wakefulness (or sleep) for more than a few hours. In other words, it reflects 'state instability' with most of the symptoms reflecting an intrusion of sleep elements into wakefulness. For example, visual hallucinations and cataplexy are due to dream imagery and REM sleep paralysis, respectively, occurring when the subject is still awake.

Cataplexy is an extremely specific symptom very rarely seen outside of narcolepsy. It is present to varying degrees in over 60% of narcoleptics, in whom it usually occurs during emotional situations. Laughter in the relaxed presence of friends or family is the commonest trigger, although some report that anticipation of a positive emotion proves to be the most effective precipitant. For example, some narcoleptics have partial attacks in which they cannot reach the punchline of jokes without becoming tongue-tied or

frankly dysarthric. Full blown cataplectic episodes usually start with irregular jerking of the face or head with eye closure but retained awareness. There is subsequent descending paralysis such that the subject slumps to the floor as the knees give way. Because attacks evolve over two or three seconds and narcoleptics usually recognise situations in which they are vulnerable, injury is rare. Similarly, episodes are not generally seen in dangerous or life-threatening situations, presumably because other arousal systems intercede. A variety of emotions can act as triggers including (pleasant) surprise, frustration and anger. However, one should be careful not to over-interpret mild symptoms of knee buckling in extreme laughter or, indeed, anger as this probably reflects a normal reaction.

The nature of the excessive daytime sleepiness in narcolepsy is usually characteristic. It is described as 'irresistible' and invariably worse if the subject is unoccupied or bored. Short naps are generally restorative and may contain dreams or hallucinatory experiences. Most narcoleptics will admit to having dropped off in unusual situations. A recent extreme example that comes to mind was a young car mechanic who fell asleep whilst bent over the open bonnet of a car with the engine running!

Vivid or unusual dreams at night due to REM sleep fragmentation and other nocturnal phenomena are also very common. Many narcoleptics report that they can control their dreams to some extent. Indeed, some develop unusual notions that they have paranormal powers and can predict the future. Distinguishing dreams from reality can also be difficult and may produce embarrassing situations. Other nocturnal symptoms such as sleep paralysis are not particularly discriminative symptoms. However, if sleep paralysis occurs as the subject is falling asleep, rather than at the point of waking, narcolepsy should be considered. In keeping with the notion of "state instability", many narcoleptics wake frequently through the night for no apparent reason and may even have difficulty dropping back to sleep. The full gamut of parasomnias is also relatively common in narcolepsy and includes arousal disorders, sleep talking and dream enactment.

It seems likely that there are subtle metabolic abnormalities in narcolepsy and it is always worth asking about appetite control and the possibility of an eating disorder. Many subjects report cravings for sweet foods in particular which can produce bingeing, especially at night. Narcoleptics tend to be overweight, it seems at least partly as a consequence of altered appetite control.

Finally, from the history, it is worthwhile exploring the concept of 'automatic' behaviours. Most narcoleptics complain that they are 'switched off' for most of the day, unable to focus, concentrate or take in information effectively. As a result of this, brief so-called 'micro-sleeps' are common such that subjects perform complex tasks including writing without full awareness or control. Placing objects in bizarre places or simply losing items around the house are particularly common examples of this.

Because narcolepsy can be disabling and is generally life-long, some authorities suggest that confirmatory tests are mandatory before treatment is started. This is debatable, especially if appropriate resources are scarce, although investigation is often appropriate in cases where the history is not classical and particularly if cataplexy is absent. The recently published criteria for diagnosing narcolepsy seem clear-cut in that a positive diagnosis is achieved when CSF levels of hypocretin are less than 110pg/ml or if the subject falls asleep in under eight minutes, on average, in a



**Dr Paul Reading, MA, FRCP, PhD,** is a consultant neurologist based at the James Cook University Hospital, Middlesbrough. He has trained in Cambridge, Edinburgh and Newcastle. Over the last seven years he has developed an academic and clinical interest in sleep medicine and been secretary of the British Sleep Society for four years. Narcolepsy and the sleep disorders associated with neurodegenerative disease are particular areas of interest.

### Correspondence to:

Dr Paul Reading,  
Department of Neurology,  
The James Cook University  
Hospital,  
Middlesbrough, TS4 3BW, UK.  
Email: Paul.Reading@tees.nhs.uk

### Key references for further reading

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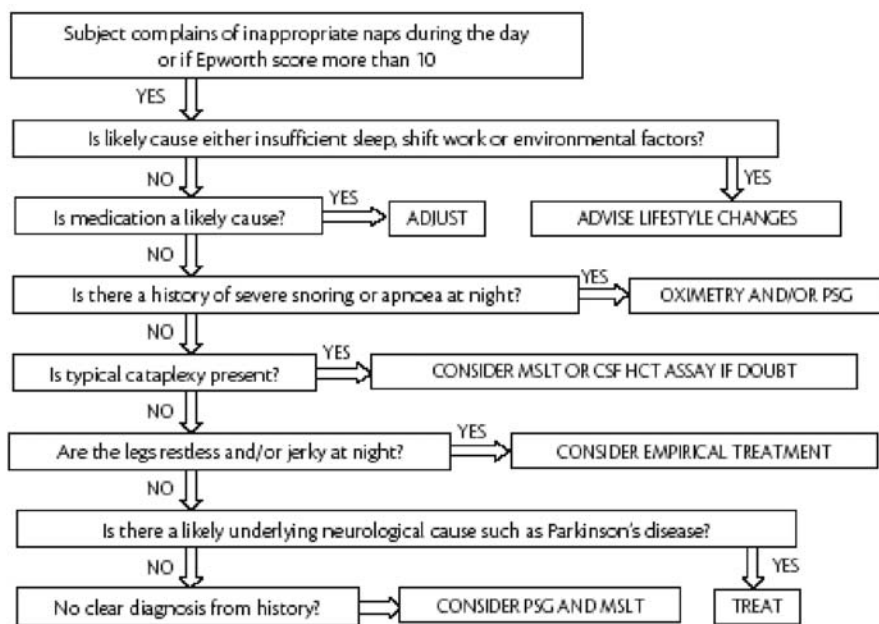


Figure 1: Algorithm for assessing subjects with excessive sleepiness. Oximetry can usually be performed in the home setting. PSG – polysomnography; MSLT – multiple sleep latency test; CSF – cerebrospinal fluid; HCT – hypocretin (also called orexin).

multiple sleep latency test (MSLT) and achieves REM sleep in at least two of the nap opportunities. Unfortunately, at a practical level, these tests are not always very helpful in cases where there is clinical doubt from the history. For example, hypocretin CSF levels may be preserved in mild or atypical cases and, in any case, reliable assays are offered by very few centres. Determining hypocretin levels can be useful, however, if results from a MSLT are surprising or if there are problems with interpretation. It is also useful in diagnosing childhood narcolepsy.

The MSLT is a notoriously fragile investigation and prone to producing false negative results. This is probably because most centres performing the test do not have particular expertise or, indeed, interest in sleep investigations and rarely have strict protocols. Several studies have demonstrated the widely varying results that can be obtained from a MSLT, depending purely on the advice given to the subject or the nature of their activities between nap opportunities. From a diagnostic perspective, I believe a convincing history should hold sway over a 'negative' MSLT.

Given that a very high proportion of narcoleptics have a DQ1B\*0602 histocompatibility haplotype, many clinicians believe that HLA testing has an important role in diagnosing narcolepsy. I think this is very rarely the case as I have seen numerous cases of DQ1B\*0602-positive sleepy people who are not narcoleptic and a smaller number of 'negative' patients with definite narcolepsy who have turned out to be hypocretin deficient. Despite its relative ease, it is simply not a specific or sensitive enough test to be of general use.

### Other causes of excessive sleepiness

A brief algorithm is provided for assessing somnolent patients (Figure 1). Most sleep experts will claim that an identifiable cause will be found for the majority of sleepy subjects, even if it turns out that they are simply 'overdoing it'. Certainly amongst respiratory physi-

cians, the Epworth score is used as a screen to differentiate sleepiness from chronic fatigue, for example, and scores over 10 are usually deemed worthy of further assessment. In my opinion, the most useful discriminatory stem question from the Epworth scale is the one that asks about typical levels of sleepiness if a subject is a passenger in a car for an hour or more. In most populations, the commonest cause of significant daytime somnolence is obstructive sleep apnoea which effectively produces symptoms by severely disrupting overnight sleep. In the typical clinical setting with a good history from a bed partner or family member, the diagnosis



Figure 2: A T2 weighted axial image (top) revealing an arachnoid cyst in the region of the third ventricle in a 45 year-old male patient presenting with excessive sleepiness, headaches and likely cataplexy. Sagittal views (bottom) demonstrate likely compression of the hypothalamus which may well account for his apparent secondary narcolepsy.

is generally straightforward and, as such, patients rarely present to neurologists. However, if the subject is not particularly overweight or if there is no corroborative history, it can easily be missed. Furthermore, it can occur as co-morbidity in patients with other diagnoses, including narcolepsy. If a patient admits to long but unrefreshing sleep and wakes with a dry mouth, feeling 'hungover', it is almost always appropriate to arrange at least overnight oximetry to explore the possibility of significant nocturnal hypopnoea or apnoea.

If narcolepsy is being considered but the history is not clear cut and cataplexy is absent, for example, the somewhat enigmatic diagnosis of idiopathic hypersomnia often needs to be considered. Typical cases are fairly rare compared to narcolepsy and are characterised by long but unrefreshing overnight sleep that appears ostensibly normal even when monitored in a laboratory setting. The main complaint is usually an extreme difficulty getting up in the morning and a subsequent propensity to long daytime naps. There are no symptoms suggestive of abnormal REM sleep mechanisms in contrast to narcolepsy. Diagnostic criteria require a sleep latency of less than eight minutes. Controversially, idiopathic hypersomnolence is now recognised as occurring with and without long overnight sleep. A number of commentators suggest that the latter category might, instead, reflect a form of monosymptomatic narcolepsy.

Most other causes of daytime somnolence can be attributed to poor quality overnight sleep. Of these, perhaps the most important treatable diagnosis is restless legs syndrome (RLS) and associated periodic limb movement disorder. RLS is a clinical diagnosis and, relatively unusually, both a cause of insomnia and daytime somnolence. If symptoms are severe, a therapeutic trial of a drug before bed is usually warranted, if only for a short period. Occasionally, in the absence of RLS and even if a bed partner is not aware of excessive movement, overnight tests pick up significant periodic leg movements or jerks that can be shown to partially arouse the sleeping subject. Given a number of potentially effective treatment options, this is a relatively rare situation in which overnight polysomnography can be extremely helpful, albeit often in retrospect.

A number of neurological patients will complain of troublesome somnolence and, assuming that breathing-related disorders have been excluded, it is debatable whether thorough investigation will aid management. Examples include patients with parkinsonism, myotonic dystrophy and multiple sclerosis. In many such patients, the ultimate cause of their somnolence is likely to be multi-factorial and an empirical approach, perhaps using wake-promoting agents, is probably justified if symptoms are troublesome. Occasionally, there will be patients with no underlying diagnoses or clues as to the cause of their somnolence. In these, a relatively low threshold for brain imaging is recommended as the author has occasionally picked up otherwise asymptomatic pathologies such as arrested hydrocephalus, arachnoid cysts in the region of the third ventricle (see Figure 2), and various hypothalamic lesions as likely substrates for the sleepiness.