Neurological sleep medicine: a case note audit from a specialist clinic

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On average, humans sleep for a third of their lives, and sleep disorders are common and treatable. However, services for most sleep disorders are highly variable across the UK, and sleep medicine is neglected in the medical curriculum. We report the findings of an audit of patients with neurological sleep disorders seen in a combined cognitive neurology and sleep disorder clinics over a seven-year period, 75 with hypersomnias, 67 with parasomnias and 39 with insomnia. Also, the results of a pilot of a cognitive behavioural therapy service for insomnia undertaken in the same population are analysed.

Sleep medicine remains a neglected area in the UK. Although neurological sleep disorders are collectively common, often highly treatable and make a major impact on the lives of sufferers, they are neglected in the undergraduate curriculum. The economic burden of sleep disorders is estimated to be £50 billion annually in the UK. There is no standard treatment pathway, with referral variously to respiratory, neurological, psychiatric and sleep centres as available. An informal survey in 2016 identified only 19 sleep disorder clinics around the UK, run by neurologists. In this paper we report an audit of the work of such a clinic and a linked pilot study of a cognitive behavioural therapy service for insomnia.

The aim is to introduce those unfamiliar with sleep neurology to the key features of these fascinating conditions. We highlight innovative treatments, such as the use of sodium oxybate (SO) for narcolepsy and of cognitive behavioural therapy for insomnia (CBTI), and the potential to develop services for patients with neurological sleep disorders within the NHS. We emphasise the striking benefits to health available from accurate diagnosis and appropriate management in this patient group. We also draw attention to some areas of difficulty and uncertainty in this highly rewarding but underdeveloped area of medical practice.

The limited services for sleep disorders in the UK reflect the lack of relevant education in the medical curriculum. Figure 1 shows the growing number of referrals to our sleep disorder clinics following the launch of an annual sleep education meeting in 2014. This self-funding meeting – ‘Waking up to sleep’ – was attended by a range of medical professionals in primary and secondary care, as well as members of the public, addressed by local and national experts. It provided a wide-ranging review of the disorders we discuss in this paper. We are responding to the growing number of sleep clinic referrals by establishing a dedicated sleep clinic and creating a clinical physiologist sleep specialist role to support the consultant in clinic and enhance care for complex cases.

Methods

Using the notes of all patients referred to our neurological sleep
disorders clinic from 2006 to 2013 (n=181), we classified the presenta-
tions into three main groups:
i. disorders causing excessive sleep-
iness, hypersomnias (n=75)
ii. disorders causing insufficient or
unsatisfying sleep, insomnias
(n=39) and
iii. disorders involving abnormal
 behaviour or experience during
sleep, parasomnias (n=67).

Here we focus on the most com-
dinons disorders within each
category:
i. narcolepsy (n=36) and idiopathic
hypersomnia (n=39)
ii. chronic psycho-physiological
insomnia (n=35), and
iii. the slow wave sleep arousal dis-
order – sleepwalking (n=42), REM
behaviour disorder (n=11) and iso-
lated sleep paralysis (n=14).

We used a **proforma** to capture the
patients’ demographic and present-
ing features, including principle
symptoms, examination findings, investigation results, treatment and
treatment response during the
audit period from 2006 to 2013. We
also report the results of a pilot
CBTI service for chronic insomnia
which ran from June 2013 to Sep-
tember 2014.

### Table 1. Clinical features, investigations and treatment in narcolepsy

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Excessive daytime sleepiness (EDS)</th>
<th>Cataplexy</th>
<th>Additional features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>Recurring bouts of sleepiness daily for at least 3 months (always present) Epworth sleepiness scale (ESS) score typically in the high teens or above (11+ is significantly sleepy)</td>
<td>Episodes of bilateral loss of muscle tone, associated with intense emotion especially laughter (present in 75% patients)</td>
<td>Broken nocturnal sleep Hypnagogic hallucinations (vivid imagery at sleep onset) Sleep paralysis Automatic behaviour</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Multiple Sleep Latency Test (MSLT)</td>
<td>Polysomnography</td>
<td>CSF hypocretin (orexin) level testing</td>
<td>HLA typing</td>
</tr>
<tr>
<td>4 opportunities are given to fall asleep during the day after a polysomnography (PSG) recording Mean latency &lt;8 minutes and early entry into REM sleep (&lt;15 minutes) in at least two naps diagnostic of narcolepsy</td>
<td>Performed to ensure there is no major abnormality of night-time sleep prior to MSLT</td>
<td>&gt;200pg/ml normal &lt;50pg/ml diagnostic of narcolepsy In most cases narcolepsy is caused by loss of hypocretin neurons, resulting in low levels of hypocretin, which is required to stabilise the sleep wake cycle'</td>
<td>Circa 90% frequency of DQB1-0602 in narcolepsy population However, this test is non-specific with DQB1-0602 in 18–35% of the general population, and in about 24% of Idiopathic hypersomniacs4</td>
</tr>
</tbody>
</table>

### Treatment/ interventions

<table>
<thead>
<tr>
<th>Drugs for EDS</th>
<th>Drugs for Cataplexy</th>
<th>Sodium oxybate</th>
<th>Non-pharmacological management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1\textsuperscript{st} line: Modafinil – wakefulness promoting agent, stimulates hypothalamic systems. Adverse effects include headache and low mood 2\textsuperscript{nd} line: Dexamfetamine – more potent stimulant than modafinil but greater potential for adverse effects, ie hypertension Pitolisant is a recently licensed stimulant, not used in our series</td>
<td>Suppress REM sleep and reduce cataplexy: only clomipramine is licensed for this use but other antidepressants including fluoxetine and venlafaxine are used</td>
<td>3\textsuperscript{rd} line: Sodium oxybate – acts on GABA and GHB receptors, consolidates night time sleep, reduces EDS and cataplexy. Currently expensive but highly effective. Side-effects include sleepwalking, enuresis, exacerbation of obstructive sleep apnoea, respiratory depression (especially with alcohol)</td>
<td>Sleep hygiene Planned naps Drug holidays: periods of 1–2 weeks during which patients stop taking medication</td>
</tr>
</tbody>
</table>
Assessments used in the clinic

The Epworth Sleepiness Scale (ESS) provides a useful measure of sleepiness. A score of 11 or above indicates excessive daytime sleepiness (EDS). While originally created for obstructive sleep apnoea, the Epworth score has been shown to be valid in assessment of narcolepsy.

In the pilot of CBTI, quality of sleep was assessed with the Pittsburgh Sleep Quality Index (PSQI). The instrument has 19 items covering common causes and symptoms of poor and disrupted sleep, which are aggregated into a single score. A global PSQI of 5 or less indicates a good sleep quality, while a score greater than 5 is indicative of a poor sleep quality. This questionnaire is validated to assess patients with insomnia and can be used to monitor the effectiveness of insomnia treatments.

Polysomnography involves the comprehensive assessment of overnight sleep, usually in a sleep laboratory, including electroencephalography (EEG) and measurement of eye movements, muscle tone, limb movements, electrocardiography and respiratory function. The Multiple Sleep Latency Test (MSLT), used to assess the degree of daytime sleepiness, allows participants four opportunities to fall asleep and monitors the latency and characteristics of any ensuing sleep.

Results

Hypersomnias – narcolepsy and idiopathic hypersomnia

Narcolepsy is characterised clinically by the tetrad of excessive daytime sleepiness, cataplexy, hypnagogic hallucinations and sleep paralysis, often associated with broken nocturnal sleep. It is generally caused by the loss of the hypothalamic neurotransmitter, hypocretin, which stabilises sleep and wakefulness. Its estimated prevalence is 0.02–0.05%. Current understanding and guidelines are summarised in Table 1.

Our audit identified 36 patients with narcolepsy across a broad age range (21–71 years), with a female preponderance (24 vs 12 male). Onset was before 30 years of age in 88% (Figure 2). Excessive daytime sleepiness was always present, cataplexy the second most frequent feature (Figure 3), and...
laughter the most common precipitant of cataplexy (Figure 4).

**Diagnosis of narcolepsy**
Narcolepsy is typically associated with EDS and cataplexy, and either a positive MSLT, or low cerebrospinal fluid hypocretin levels. Some 17% of our patients were not cataplectic but could be diagnosed based on the other key symptoms and investigations. The MSLT was an insensitive diagnostic tool: of 26 patients tested, 12 had a mean sleep latency of <8 minutes, nine exhibited two or more sleep onset rapid eye movement (REM) sleeps, and six displayed both. In contrast, cerebrospinal fluid (CSF) hypocretin levels were diagnostic in 11 of 12 patients tested.

**Treatment of narcolepsy**
Excessive daytime sleepiness in narcolepsy was treated with stimulants, primarily modafinil (30 of 36) and dexamfetamine (13 of 36). These provided satisfactory control of symptoms in 43% and 28% of patients, respectively. Sodium oxybate (Xyrem) was used only in patients with severe symptoms refractory to other drugs, and was strikingly effective: 9 of 11 patients reported major benefit, with a mean fall in the ESS of 10.5 points. Several sodium oxybate-treated patients were able to return to school or work.

Cataplexy in narcoleptics was treated with a range of antidepressants, benefitting approximately one half of our patient group.

**Idiopathic hypersomnia**
Idiopathic hypersomnia (IH) refers to EDS in the absence of insufficient sleep or any other evident medical explanation, such as narcolepsy or obstructive sleep apnoea. During the sampling period 39 patients presented in this way with a mean ESS score of 15.8 (range 11–20). Polysomnography was normal in 17 of 18 cases tested, one patient showing periodic limb movements of sleep. The age of onset was more evenly distributed than in narcolepsy, but still clustered under 30 years (Figure 5). Clinical features associated with narcolepsy were rare, and cataplexy was absent (Figure 6).

**Chronic psycho-physiological insomnia**
People with insomnia sleep poorly despite good opportunity to sleep (detailed features in Table 2). It is the most common of the sleep disorders, with estimated prevalence of 10–50% depending on population and definition. Insomnia can have a major impact on everyday activities, performance at work and quality of life. It is more common in older people, women, shift workers and those with pre-existing medical or psychiatric illnesses. Persistent insomnia increases the risk of...
depression, and can lead to chronic use of hypnotics and alcohol. Insomnia patients often describe the condition as being very lonely and have a sense of hopelessness and desperation.

Among 39 patients referred because of insomnia, 35 satisfied criteria for chronic insomnia. Their mean age was 44 years, and 54% were female. At presentation the mean duration of their insomnia symptoms was 19.5 years. Forty-four per cent had maintenance insomnia, 23% initial insomnia, and the remaining third had mixed insomnia. The mean ESS was 7.95, indicating that most patients with insomnia were not excessively sleepy during the day, a common finding in chronic insomnia.

**Treatment of insomnia**

CBTI is a specialised form of cognitive behavioural therapy requiring specific training in behavioural sleep medicine. Arthur Spielman and Richard Bootzin developed the main components of CBTI12,13. CBTI focuses on building the sleep drive to encourage sleepiness at the right time of day (sleep restriction therapy), correcting inaccurate beliefs about sleep, breaking the association between the bedroom and wakefulness, winding down successfully and reducing anxiety. This is done by using a combination of evidence-based techniques requiring patients to change certain behaviours and thought processes surrounding their sleep. CBTI is usually delivered in four sessions, either in groups or one-to-one. Sleep diaries are often used to aid this process. CBTI is safe and successful for most patients, but when implementing strategies such as sleep restriction therapy where sleepiness needs to be built up, it is important to know if patients already have excessive daytime sleepiness, seizure disorders or significant mood disorders that may be affected by further sleep deprivation. Appropriate supervision by trained CBTI specialists is required for this aspect of treatment. The treatment requires commitment, as patients need to engage and to comply with the strategies consistently. The main objective of CBTI is to improve the patient’s perceived and objective quality of sleep; often this comes with an increase in sleep time as well. At present it is not widely available in the NHS, because of lack of awareness of its proven benefits, lack of availability of trained therapists and separation of services for psychological and physical health.

**CBTI pilot**

Between June 2013 and September 2014, a sleep physiologist trained in cognitive behavioural therapy for insomnia ran a pilot service in Exeter. CBTI was offered to 51 patients, of whom 29 attended all the four sessions in the course (57%), and five patients attended in part (10%). Where patients attended the whole course, we compared them before and after (thus a per protocol analysis). Sleep efficiency averaged at 61.9% before, rising by 23.8% to 85.7% after the full course (p<10-5). Total sleep time averaged 4.9 hours before, rising by 1.5 hours to 6.4 hours after (p<10-5). PSQI scores, where under 5 suggests healthy sleep,
averaged 14.2 before, falling by -5.3 to 8.9 after (p<10^-5) (Figure 7). Previous studies have reported similar findings, with evidence of durable, long-term benefit.\textsuperscript{14}

Thematic analysis of patient feedback showed that they felt more empowered and in control of their sleep problem, less lonely and hopeless, and that their sleep problem had been validated. Other benefits included feeling more positive during the day, being more organised and more efficient day-to-day. There were no reported adverse effects. Due to the success of this pilot an ongoing service has now been commissioned.

**Parasomnias**

Parasomnias are disorders of behaviour or experience during sleep, affecting about 2–5% of the population.\textsuperscript{15} Under normal conditions our brains move between three primary states of consciousness: wakefulness, non-rapid eye movement (NREM, ranging from stages 1 to 3) and rapid eye movement (REM, characterised by especially vivid dreaming) (Figure 8). Parasomnias often involve ‘state dissociation’ in which features of one of the normally distinct sleep states intrude into another. For example, the brain of a sleepwalker remains substantially in NREM sleep, but this is associated with motor activity of the sort normally confined to wakefulness. The key features of REM sleep behaviour disorder (RBD), slow wave sleep parasomnias (including sleepwalking) and sleep paralysis are shown in Table 3. Diagnosis is usually possible without PSG but this can be helpful, for example, in confirming the loss of REM atonia in REM behaviour disorder, and in ruling in or out nocturnal epilepsy, an important differential diagnosis of parasomnias.

Our data conformed to patterns already described in the literature. SWS parasomnia showed a juvenile onset, contrasting with the onset of RBD in later life (Figure 9). RBD shows a male predominance (Figure 10). Slow-wave sleep (SWS) parasomnias occurred early in the night, whilst RBDs occurred in the second half of the night, because slow-wave sleep dominates in the first half of the night and REM sleep in the second (Figure 11).

We investigated the subjective experiences of patients with parasomnias. As expected from the literature, sleepwalkers were unlikely to recollect their behaviours. By contrast, patients with RBD can usually recall the associated dream, and those with sleep paralysis have a clear recollection of their predicament. Interestingly, despite the low frequency of recollection of among sleepwalkers, around half report experiencing imagery on at least some
occasions, often involving animals (especially spiders and snakes). Animal imagery features less prominently in the dreams of patients with RBD and sleep paralysis (Figure 12).

### Discussion

Taken together, the neurological sleep disorders are very common. While they can have a marked impact on quality of life, they are often amenable to treatment. However, services for patients with these disorders remain limited and variable in the UK. This insufficient provision is partly attributable to the lack of education about sleep in undergraduate and graduate curricula: we are currently updating a study from the late 1990s, which reported a median of less than 30 minutes sleep education in preclinical and clinical curricula. But it also reflects the lack of a coordinated approach to sleep medicine: sleep is, all too often, nobody’s business. Respiratory physicians, neurologists, general practitioners, psychiatrists and psychologists all see patients with the disorders described in this paper, but in the absence of an overarching specialism of sleep medicine, expertise is bound to be variable.

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### Table 3. Clinical features, investigations and treatments for parasomnias

<table>
<thead>
<tr>
<th>Slow-wave sleep (SWS) parasomnias</th>
<th>Sleep paralysis</th>
<th>REM sleep behaviour disorder (RBD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical features</strong></td>
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</tbody>
</table>
| ‘Confusional disorders’, occurring when the brain is partially aroused from SWS, typically in the first 2–3 hours of sleep. Manifestations include:  
  – Confused arousals: brief, partial awakenings with confused mentation  
  – Sleepwalking, ranging from movements around the bed to full ambulation  
  – Night terrors  
  – sudden episodes of intense fear and often screaming usually with amnesia of the episode  
  Onset typically in childhood | Persistence of REM atonia into wakefulness  
  Can occur when falling asleep or when awakening  
  May be associated with visual and auditory hallucinations, often of a frightening ‘presence’ in the room, a feeling of respiratory distress and (until the benign nature of the disorder is understood) extreme fear  
  Onset usually in childhood or Adolescence | Dream enactment behaviour occurring in REM sleep, usually in the second half of the night. The dream is typically well recalled after the episode and is often violent  
  There is loss of normal REM atonia (allowing movement and vocalisation during REM)  
  Often (>80%) a precursor to a synucleinopathy, typically Parkinson’s disease, after an average interval of circa 10 years  
  Onset usually >50 years, male predominance |
| **Expected findings on PSG**       |                |                                   |
| Not always performed, but EEG may show arousals from slow wave sleep. Video recording captures related behaviours | Not usually performed | History alone may be diagnostic but when required PSG shows evidence of excessive muscle activity during REM |
| **Treatments**                     |                |                                   |
| Weak evidence for value of clonazepam and paroxetine. Keep sleeping environment safe  
  Avoiding sleep deprivation  
  Avoiding alcohol  
  Basic safety precautions to avoid injury during episodes | Not usually treated pharmacologically  
  Explanation and reassurance  
  Avoiding sleep deprivation and alcohol | Clonazepam first-line, melatonin and dopamine agonists sometimes useful (lack of robust evidence: see main paper). Keep sleeping environment safe |

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### Figure 9. Age of onset of SWS parasomnias, REM sleep behaviour disorder and sleep paralysis

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>Slow-Wave Sleep parasomnias</th>
<th>REM sleep Behaviour Disorder</th>
<th>Sleep paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–9</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>10–19</td>
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<td></td>
<td></td>
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<tr>
<td>20–29</td>
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<td></td>
<td></td>
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<tr>
<td>30–39</td>
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<td>40–49</td>
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<td>50–59</td>
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<td></td>
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<td>60–69</td>
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<td>70–79</td>
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www.progressnp.com
Two of the advances highlighted in this paper illustrate the problem. Xyrem is an evidence-based and highly effective,7 if expensive, treatment for narcolepsy. Its availability is very inconsistent. A small number of hospitals with sleep centres have agreed prescribing guidelines for Xyrem with local clinical commissioning groups.16 The Department of Health has agreed to pay for Xyrem in selected cases where the disorder appears to be linked to flu vaccination using Pandemrix.17 However, most patients in need of Xyrem depend on the system of ‘individual funding requests’, which, in the authors’ experience, leads to rare and unpredictable funding for the drug.18 A better integrated national service for patients with neurological sleep disorders would help to reduce such inconsistent provision.

CBTI is a promising, evidence-based treatment, of the kind recommended by NICE in the management of long-term insomnia.11 Compared with Xyrem, it is relatively inexpensive once provision is established. A small number of therapists have received appropriate training but, to our knowledge, very few hospitals in the UK currently provide a CBTI service routinely. Our own experience following a successful local pilot was that establishing a routine CBTI service was challenging. This is partly because a psycho/behavioural approach to a neurological problem, provided in this case by a sleep physiologist, did not fit easily into the established systems of secondary care. We are delighted that the service has now been adopted.

Finally, while there are several effective treatments for neurological sleep disorders, there is a dearth of high quality evidence for many approaches currently in use. For...
example, the use of clonazepam in RBD and SWS parasomnias relies substantially on anecdotal evidence. We hope that this paper will contribute in a small way to stimulating the growth of sleep medicine in the UK, benefitting services for, and our understanding of, this fascinating and therapeutically rewarding group of disorders.

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Declaration of interests
No conflicts of interest were declared.

References