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Sleep physiology and the perioperative care of patients with sleep disorders

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Key points

- Obstructive sleep apnoea (OSA) is a common condition that remains undiagnosed in many subjects and is associated with increased perioperative airway, respiratory, and cardiovascular complications.
- The STOP-BANG Questionnaire is a simple eight-point patient-administered screening tool that is useful in detecting those at risk of OSA. A score of ≥5 indicates a high probability of moderate or severe OSA.
- Day-case surgery may be reasonable in patients with OSA, depending upon severity, the presence of co-morbid conditions, and the nature of the proposed procedure.
- Consideration should be given to managing patients at risk of OSA with a local or regional technique.
- Patients with narcolepsy and other conditions causing significant excessive daytime sleepiness may be treated with stimulant medication that has a sympathomimetic potential.

Sleep is a normal physiological process that is of great importance to us all. We know when we have not had enough of it and are aware of the effects that this can have on not only our work and productivity, but also on our social lives and emotional well-being. In addition to sleep deprivation-related personal accidents, it is well established that there is also an adverse effect on complex, 'executive' decision-making abilities, something that should concern us in our professional roles.

Sleep has fascinated man throughout the ages. It is not difficult to see why early thinkers considered sleep to be a dormant process, somewhere between wakeful, sentient life, and the permanent state that is death. In Greek mythology *Hypnos* is the personification of sleep, his twin is *Thánatos* (death) (Fig. 1).

However, this long-held idea of dormancy conflicts with man's equally long-held fascination with the process of dreams and the idea (or 'science') of dream interpretation. A link with spirituality was an easy conclusion for early thinkers. Sleep and dreams rival love and war as age-old favourites for musings, poetry, and full philosophical debate. According to biblical legend, Joseph was asked to interpret Pharoah's dreams. More recently Shakespeare, in Hamlet's famous soliloquy, expounds 'To die, to sleep, to sleep perchance to dream' and 'For in that sleep of death, what dreams may come'.

As a physiological discipline, the study of sleep is relatively new. This is in part attributable to the prolonged anti-social hours associated with direct observation. The effects of sleep deprivation were observed by Kleitman in the 1920s. Berger described electrical activity in the brain in 1928, first, distinguishing between patterns seen in the wakeful and sleeping states. However, it was still believed that sleep was analogous to an idling dormancy. Rapid eye movement (REM) sleep was not discovered until 1952. Dement and Kleitman went on to discover sleep cycles whereby a predictable pattern of relatively easily measurable electrical activity occurs across the night. This became the subject of much interest in the 1960s when a greater understanding accelerated and sleep medicine as a medical speciality was 'born'.[1] In 1968, Rechtschaffen and Kales[2] described a reporting/scoring system for describing sleep that remains fundamental to physiological research and clinical investigation today. This 'R&K system' was used until 2007 and has been just slightly modified since then. The method used to fully document the sleep process is called 'Polysomnography' (PSG). The name relates to the

Fig 1 'Sleep and his half-brother death'. J.W. Waterhouse, 1874. Image courtesy of Sotheby's, Inc. © 2003.

measurement and recording of many physiological variables during sleep. This includes electro-encephalography (EEG), electro-oculography (EOG), electro-myography (EMG: usually submentalis and tibialis anterior muscles), ECG, pulse oximetry, thoracic and abdominal effort (using impedance bands), and oral and nasal air flow (with a thermistor or pressure sensor worn on the top lip). Additionally, an infra-red camera is included to observe complex motor behaviour and to allow visual monitoring by technical staff from a remote room. Figure 2 shows a brief segment from a PSG recording.

Normal physiology

The exact nature of sleep remains elusive, but it is clearly important since we cannot survive without it. Sleep is consistently recognized in all 'higher organisms' studied. Even insects can be observed to have a circadian activity/inactivity cycle. Our sleep can be broadly divided into REM sleep and non-REM sleep. On passage from the waking state to Stage 1 non-REM sleep, the EEG frequency decreases while its amplitude increases. This phenomenon continues as sleep deepens though Stages 2 and 3 to Stage 4 non-REM sleep. Additionally, other EEG phenomena are seen in Stage 2 (K-complexes and sleep spindles). Stages 3 and 4 are also known as slow wave sleep (SWS) and are now commonly reported together as Stage N3 sleep. REM sleep is characterized by a higher frequency lower amplitude pattern that resembles the waking state. However, there is also the presence of rapid flicking eye movements that give a characteristic appearance to the EOG along with a generalized reduction in muscle tone evident on the EMG. REM sleep contains significant dreaming and in simple terms, this atonia stops us acting out dream-related movements.

Sleep is scored by dividing the night's recording into consecutive 30 s epochs. A score is given to each epoch that represents the predominant stage contained (wake, N1, N2, N3, or REM). These epochs can then be visually represented as a 'hypnogram' that shows sleep stage changes across the night (Fig. 3).

Typically, a 7–8 h night of sleep is made up of 4–5 sleep cycles, each of ~90 min. In a healthy young adult, the first cycle is usually deep with a significant period of SWS (N3) followed by a lightening through N2 to a brief period of REM sleep. Each subsequent cycle is less deep and followed by a greater proportion of REM sleep such that by the fourth or fifth cycle there is no SWS, but a prolonged REM period containing the dreaming sleep that we so readily recall on waking. With increasing age, normal sleep becomes more fragile with little or no SWS and more frequent interruptions to the waking state across the night.

Pathophysiology sleep disorders

The range of known sleep disorders is set out in an internationally agreed classification system.[3] Broadly speaking, these can be divided into difficulty sleeping (insomnia), difficulty staying awake (hypersomnia, which may be primary or secondary), being asleep or awake at the wrong time of the day (circadian rhythm disorders) or abnormal/unwanted behaviours or movements in sleep (parasomnia). Each category contains a range of different defined conditions.

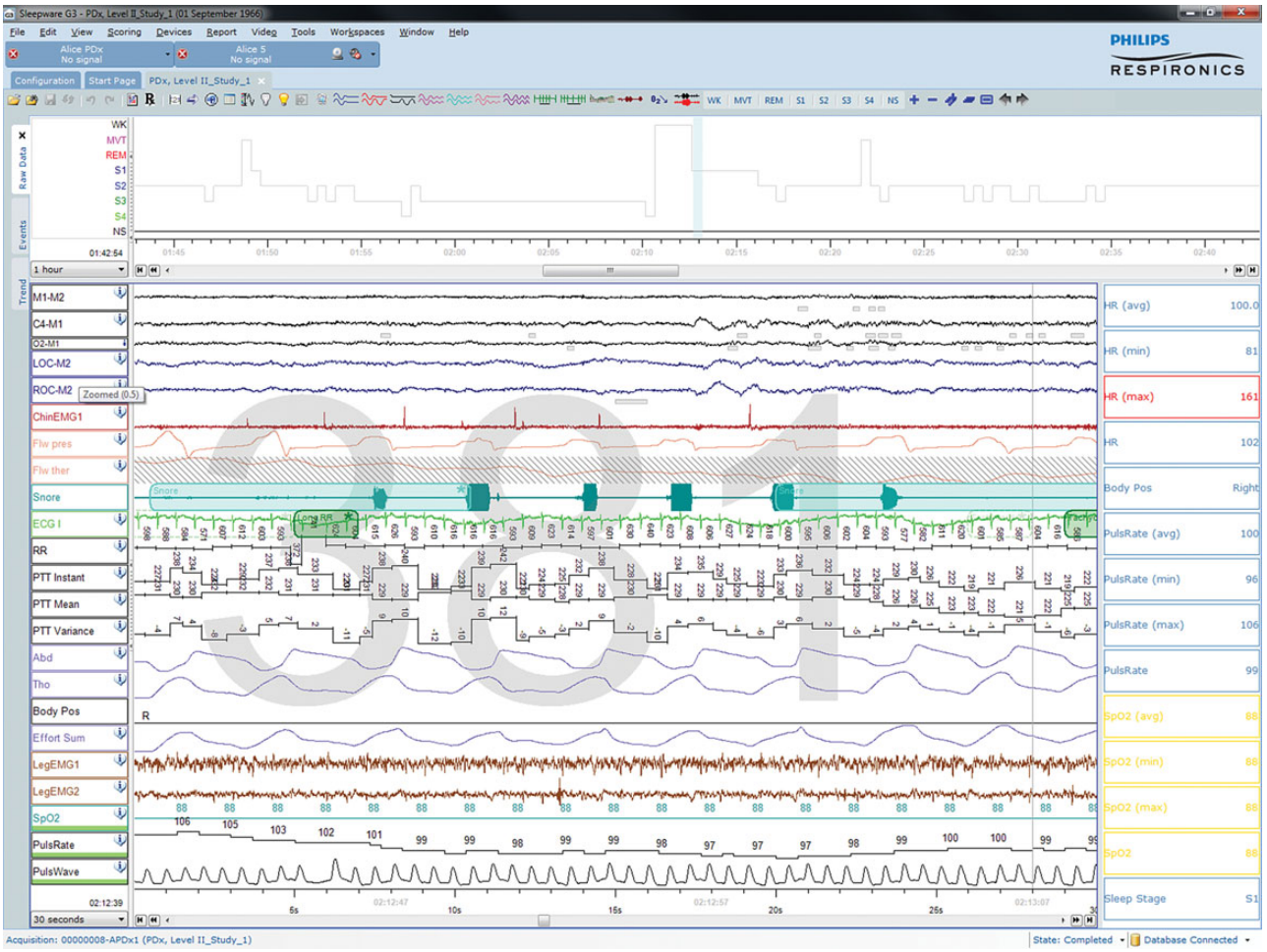

Fig 2 A 30 s 'epoch' of PSG recording.

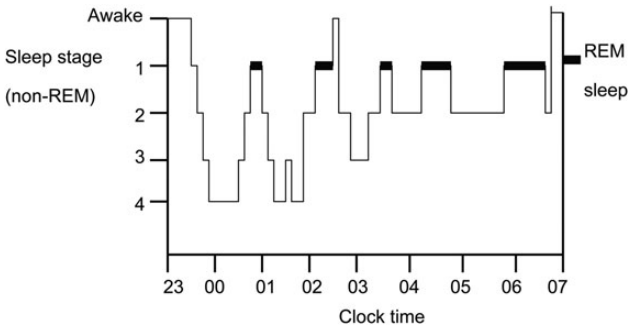

Fig 3 Typical hypnogram of a healthy young adult.

Insomnia is the commonest sleep problem though is generally managed in primary care. Circadian rhythm disorders and Parasomnias may require more specialist input for investigation and diagnosis. Parasomnias vary from simple confusional arousals, sleep walking, and talking to severe nightmares, night terrors, and more complex motor behaviour that may include basic human functions such as eating and sexual activity and even interaction with technology such as driving a car. There are several rare and unusual conditions in this category. For example, Exploding Head Syndrome, whereby the subject perceives the sound of a violent explosion usually at, or shortly after sleep onset. This is understandably a very frightening experience. Though poorly understood, it is entirely benign.

Hypersomnia generally requires more specific investigation. Treatment regimens and some diagnoses may be of some relevance to the practice of anaesthesia (see below). Primary hypersomnias consist of conditions of central (brain) origin and include narcolepsy and also idiopathic hypersomnia (which as the name would suggest, is a diagnosis of exclusion). In narcolepsy there is thought to be an acquired defect in a 'sleep control switch' that has been shown to be HLA-linked and is probably immune-mediated. Perhaps akin to the loss of pancreatic β-cells in Type I diabetes mellitus, there has been shown to be a deficiency of cells in an area of the hypothalamus that produce orexin/hypocretin (a polypeptide neurotransmitter). In a canine model of narcolepsy, the defect has been shown to be in the orexin/hypocretin receptor. Broadly, a fragmented night of shallow sleep results in significant daytime sleepiness and other sleep-related phenomena such as sleep paralysis, hypnogogic and hypnopompic hallucinations (vivid and often disturbing dreams at sleep onset and offset) and in some individuals, cataplexy. Cataplexy is a brief loss of muscle tone that would be normal in REM sleep, but occurring in the waking state and generally provoked by emotional extremes such as laughter and anger.

It is not surprising that other conditions leading to disturbed and fragmented sleep can render the individual sleepy in the day time. 'Secondary' hypersomnias include Sleep Disordered Breathing and Restless Legs Syndrome/Periodic Limb Movements in Sleep; non-central (non-brain) factors that disturb and fragment sleep. More mundane external factors are legion and might also include reduced opportunity for sleep because of poor sleep hygiene (essentially 'burning the candle at both ends').

Sleep disordered breathing can significantly disturb sleep and the term includes a number of conditions such as Obstructive Sleep Apnoea (OSA), sleep apnoea states of central origin and hypoventilation/hypoxaemia because of a variety of pulmonary parenchymal, vascular, neuromuscular, or chest wall disorders. Significant obesity causing obesity hypoventilation syndrome (OHS) is included here. However, these are relatively rare and I will therefore concentrate on OSA.

Obstructive Sleep Apnoea

Snoring is very common. Most of us do it from time-to-time and it is more likely when lying supine or after alcohol. Snoring is produced by the vibration of tissues of the pharynx when inspiratory effort against a relatively obstructed airway causes upper airway narrowing and collapse. Complete obstruction results in an apnoeic episode, defined as a 10 s absence of flow. Partial obstruction may cause a hypopnoea whereby flow is halved over a 10 s period. Both result in a dip in arterial oxygenation. Obstructive events result in partial arousal from sleep causing sleep fragmentation and are associated with an increase in sympathetic activity with increases in heart rate and blood pressure. This may result in excessive daytime sleepiness and a sustained increase in adreno-cortical tone. Paradoxical hypertension may be seen whereby individuals have a higher nocturnal than daytime arterial pressure.

For an adult, up to five apnoeic or hypopnoeic events per hour are considered to be within normal limits. Whereas apnoea-hypopnoea indices (AHI) of 5–15, 15–30, and >30 events per hour represent mild, moderate, and severe OSA, respectively. In the UK, suspected OSA is generally diagnosed using outpatient investigation. A full inpatient PSG study is labour-intensive and therefore expensive. Outpatient home respiratory studies use either pulse oximetry alone or oximetry plus airflow and abdominal-thoracic effort monitoring to give an oxygen desaturation index (ODI) or ODI plus AHI assessment. There is generally good agreement between the AHI and the ODI (whereby a 4% dip is used for definition). Though the threshold for diagnosing severe OSA is 30 events per hour, it is not unusual to see patients with an AHI or ODI of 60 or more whose average oxygen saturation across the night is <90%. In markedly obese individuals, there is a considerable overlap of OSA with OHS. These individuals experience significant hypoxia in sleep, but also retain CO_2. Right heart failure may also be evident.

OSA: perioperative concerns

As anaesthetists we commonly direct much attention to ensuring that our patients have oximetry-derived oxygen saturations in the mid-to-high 90s. It is therefore both interesting and worrying to see so many diagnostic results in newly referred patients with severe OSA who have average nocturnal haemoglobin oxygen saturations in the mid-to-high 80s for much of the night and in all likelihood have done so for many months or even years before being referred. Of course, these patients may require anaesthesia and it is easy to see that the addition of sedative, paralysing, and respiratory depressant medication may significantly compound their respiratory problems in the postoperative period.

The prevalence of OSA in the general population has been estimated to be between 5 and 9%. It is likely to be higher in the surgical population and particularly so among certain patient groups such as those undergoing bariatric surgery. It has been shown that many patients with OSA remain un-diagnosed despite both surgical and anaesthetic preoperative review. A recent study from a Canadian group reported that among 267 preassessed patients with moderate-to-severe OSA, 92 and 60% were not diagnosed by their surgeons and anaesthetists, respectively.[4] The incidence of postoperative oxygen desaturation, respiratory failure, cardiac events, and unplanned intensive care unit transfer are all higher in subjects with OSA.[5]

Risk factors for OSA include obesity, male gender, loud snoring, observed apnoeic episodes, and excessive daytime sleepiness. On examination, the finding of a crowded airway with an adverse Mallampati score is also significant; an independent association with the presence and the severity of OSA has been demonstrated.[6]

Various screening tools for OSA have been introduced. However, most require administration or supervision by a healthcare professional in order to be reliably completed. The STOP-BANG questionnaire (Fig. 4) has been developed and validated specifically as a preoperative screening tool. It consists of eight simple yes/no questions that most patients can self-administer. A score of 3 or more 'yes' answers has been shown to indicate a high risk of OSA though a high proportion of false-positives will be included. A score of 5–8 identifies patients with a high probability of moderate or severe OSA, the group most likely to benefit from particular attention.[7]

OSA: perioperative management

Patients with OSA may still be suitable for day-case surgery. Day-case guidelines are often controversial and may differ significantly between units on many criteria including a body-mass index cut-off point. However, the nature of surgery, proposed anaesthetic technique, and the presence of other co-morbid conditions (e.g. ischaemic heart disease, diabetes, etc.) should be considered alongside the severity of OSA and whether the patient is already established on continuous positive airway pressure (CPAP) treatment. The American Society of Anesthesiologists convened a

Snoring: Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?	Yes / No
Tired: Do you often feel tired, fatigued or sleepy during the daytime?	Yes / No
Observed: Has anyone observed you stopping breathing during your sleep?	Yes / No
Blood **P**ressure: Do you have high blood pressure or are you on treatment for high blood pressure?	Yes / No
BMI: Is your Body Mass Index greater than 35kg/m^2?	Yes / No
Age: Are you over 50 years old?	Yes / No
Neck Circumference: Is your neck circumference greater than 40cm (16 inches)?	Yes / No
Gender: Are you male?	Yes / No

Fig 4 STOP-BANG questionnaire.

Table 1 Managing patients with OSA

Preoperative assessment	• Use an appropriate screening tool such as the STOP-BANG questionnaire • Consider referral of undiagnosed moderate-to-high risk elective patients for formal sleep assessment • Consider that patients with OSA are at a higher risk of difficult intubation and may have associated co-morbid conditions such as ischaemic heart disease, hypertension, and type-2 diabetes mellitus
Preoperative preparation	• Encourage patients to make good use of their CPAP device and to bring it into hospital with them • Day-case surgery is not contra-indicated but its suitability will depend upon the nature of surgery, proposed anaesthetic technique, and post-operative analgesia requirements
Intraoperative care	• A local or regional technique is preferred where suitable • When general anaesthesia is to be used, a greater risk of difficult intubation should be anticipated • The patient should be extubated when awake
Postoperative care	• Analgesic regimes that minimize respiratory depression are preferred, especially local, or regional techniques • CPAP may be required to support the airway, with or without supplementary oxygen administration • A prolonged period of monitoring may be required, particularly when sleeping. Oximetry may be adequate though the patient should be cared for in an area where there is sufficient trained staff to recognize and manage problems

task force that developed practice guidelines for the perioperative care of patients with OSA in 2006, which were updated in 2014.[8] These are summarized in Table 1. General anaesthesia and the use of systemic opioids can be expected to compound the risk of airway obstruction in the postoperative period. While there is no clear data on relative risk in this regard, the use of local or regional techniques may offer a clear benefit.

The 'gold standard' treatment for OSA is CPAP. Most individuals with moderate-to-severe OSA take to it with great effect, rapidly realizing the improvement in their sleep quality and daytime function. However, some individuals continue to struggle and need much encouragement to persevere. Though there is no good evidence that preoperative CPAP use reduces perioperative risk, it is well established that CPAP reduces overall risk of a variety of adverse cardiovascular outcomes. Patients who use CPAP should bring their device into hospital with them. Ward staff may be dismayed by the presence and use of equipment with which they are unfamiliar. However, explanation should be simple and it would be absurd (and potentially dangerous) to deny perioperative patients a treatment that they usually self-administer at home. Many modern CPAP devices are capable of detecting obstructive events across the night and vary the delivered pressure according to need. This may minimize discomfort for the patient while providing just enough pressure to keep the airway open across the night when sleeping position and thus pressure requirements may vary. It is likely that the patient's own machine and mask will better prevent any obstructive events than a generic hospital device set to a 'best guess' fixed pressure. If supplementary oxygen is required, it may be introduced at any point into the circuit or mask. It is most convenient to add a short tube with a side port (for oxygen tubing connection) between the CPAP generator unit and the hose pipe. This avoids excessive connections and potential tangling at the mask end.

Perioperative concerns drugs used in sleep medicine

Most of the drugs used in sleep medicine are well known to the anaesthetist and include sedatives such as benzodiazepines, clonazepam, and the newer non-benzodiazepine 'Z-drugs' (Zopiclone, Zolpidem, and Zaleplon), atypical analgesics/anti-epileptics such as gabapentin and pregabalin and dopamine agonists such as ropinirole, pramipexole, and rotigotine. The latter are considered first-line agents in the management of Restless Legs Syndrome/Periodic Limb movements in Sleep, but are used in much smaller doses than in the treatment of Parkinson's Disease. Melatonin is sometimes used in subjects with circadian rhythm disorders. These can all be expected to have little or no impact upon the conduct of anaesthesia though sedatives in higher dose may compound CNS or respiratory depression.

Stimulants that promote wakefulness and other agents used in the treatment of narcolepsy may be of interest. Patients with a primary hypersomnia may use drugs such as dexamfetamine, methylphenidate, and modafinil. The latter is most commonly used and has the least cardiovascular effects, the principal concern to the anaesthetist. However, all are short acting and would not be required on the day of elective surgery or in the immediate postoperative period. There may be some concern where emergency surgery is required though this is unlikely to be as significant as that with illicit recreational stimulants such as cocaine.

Patients with narcolepsy that also have cataplexy may be taking anti-depressant drugs as anti-cataplectic agents. Clomipramine was originally popular in this regard, though more recently the non-sedating Venlafaxine is preferred as a first line agent. Abrupt discontinuation of such an agent may result in a dramatic increase in the frequency of cataplexy episodes and this can be very disabling (status cataplecticus), though it is unlikely to be dangerous.

The last decade has seen an increased use of sodium oxybate in the treatment of more severe cases of narcolepsy with cataplexy. Though there are still only a few hundred UK patients treated in this way, it deserves a special mention since the drug has previously been used as an i.v. anaesthetic agent. Though abandoned as an anaesthetic induction agent, it was noticed that it produced an EEG picture of slow wave sleep, something that is absent or poorly consolidated in subjects with narcolepsy. It has been shown to help consolidate sleep in narcoleptics, resulting in reduced daytime sleepiness and also a reduction in the frequency and severity of cataplexy episodes.

Sodium oxybate is a significant depressant agent. It should not be taken with alcohol or indeed after general anaesthesia or use of other depressant agents. However, it is very short lasting and generally taken orally in two divided doses at night; on

retiring and with a second dose after 2.5–4 h of sleep. It is safe to use on the night before surgery and can be restarted when sedative and depressant anaesthetic or analgesic effects have ceased.

Declaration of interest

None declared.

MCQs

The associated MCQs (to support CME/CPD activity) can be accessed at www.access.oxfordjournals.org by subscribers to *BJA Education*.

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