REVIEW

Clinical diagnosis and misdiagnosis of sleep disorders

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Sleep disorders are common in all sections of the population and are either the main clinical complaint or a frequent complication of many conditions for which patients are seen in primary care or specialist services. However, the subject is poorly covered in medical education. A major consequence is that the manifestations of the many sleep disorders now identified are likely to be misinterpreted as other clinical conditions of a physical or psychological nature, especially neurological or psychiatric disorders. To illustrate this problem, examples are provided of the various possible causes of sleep loss, poor quality sleep, excessive daytime sleepiness and episodes of disturbed behaviour at night (parasomnias). All of these sleep disorders can adversely affect mental state and behaviour, daytime performance or physical health, the true cause of which needs to be recognised by clinicians to ensure that appropriate treatment is provided. As conventional history taking in neurology and psychiatry pays little attention to sleep and its possible disorders, suggestions are made concerning the enquiries that could be included in history taking schedules to increase the likelihood that sleep disorders will be correctly identified.

Sleep disorders are among the most common complaints seen by general practitioners. They also complicate very many conditions referred to specialist medical services. Awareness of the wide range of codified sleep disorders is increasing, but not fast enough, considering how common such disorders are and their often serious consequences. At any one time, approximately 30% of the general public are affected by a significant sleep problem,[1] often of long standing, with much higher rates in certain groups such as the elderly,[2] those with a psychiatric disorder[3] or learning disability,[4] and others who have neurological or other medical disorders.[5] This overall pattern is true of children as well as adults.[6] Persistent sleep loss or poor quality sleep affects emotional state and behaviour, cognitive function and performance at school or work, family cohesion and general quality of life, mental health and also physical well being.[7] The total cost of these consequences in human and economic terms has been calculated to be enormous.[8]

The general public are still not particularly well informed, nor are healthcare professionals because of deficiencies in their training. A 1998 survey of UK medical schools revealed that out of a typical 5 year undergraduate course, the median time spent on formal teaching about sleep and its disorders was 5 min.[9] There is no reason to believe that the situation has improved since then, and no evidence that the deficiency is corrected in higher training, even in specialties where the prevalence of sleep disorders is particularly high, such as paediatrics, psychiatry or geriatrics. Understandably, therefore, medical staff do not usually enquire about sleep symptoms[10] and, where treatment is prescribed, there is still over reliance on medication, especially hypnotics, despite the well established drawbacks of their use.[11]

Similar shortcomings have been reported in the training of nurses[12] and clinical psychologists[13] who, in theory, are well placed to identify and, in some instances, treat sleep disorders. It is cold comfort that these shortcomings in professional training, and their consequences for standards of clinical care, are not confined to the UK but are reported in other countries, including the USA[14] where sleep disorders medicine is generally better recognised than elsewhere.

This lack of adequate attention to sleep disorders is significant because there are many important points of direct relevance between the 90 or more sleep disorders now described in the recent second edition of the *International Classification of Sleep Disorders*,[15] and other areas of clinical practice.

- As mentioned already, sleep disturbance accompanies most medical and psychiatric disorders, often adding appreciably to the patient's distress.
- Some sleep disorders have a well defined basis in medical disorder. Obstructive sleep apnoea (OSA) is a case in point, and also rapid eye movement (REM) sleep behaviour disorder (RBD), which is often a manifestation of neurodegenerative disease (see later for these conditions). Further examples are sleep related disturbed behaviours (parasomnias)[16] due to such medical conditions as epilepsy or asthma (examples of ''secondary'' parasomnias). Other parasomnias have strong psychiatric affiliations, for example nocturnal panic attacks, sleep related eating disorders, sleep disturbance in post traumatic stress disorder (mainly nightmares) as well as dissociative (including ''hysterical'') states at night.
- Certain sleep disorders carry an increased risk to the individual of developing physical and psychiatric illness.[7] For example, shift work disorder is linked with various medical conditions, especially peptic ulcer, coronary artery

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Abbreviations: DSPS, delayed sleep phase syndrome; NFLE, nocturnal frontal lobe epilepsy; OSA, obstructive sleep apnoea; RBD, rapid eye movement sleep behaviour disorder; REM, rapid eye movement

disease and also complications in pregnancy; OSA may contribute to cardiovascular disease, notably hypertension and stroke, and possibly diabetes. Persistent sleep loss, whatever its cause, has been linked with a wide range of disorders, including poor resistance to infection, as well as psychiatric conditions, especially anxiety, depression, and alcohol and other substance abuse.

- Sleep disturbance can exacerbate pre-existing medical and psychiatric disorders. For example, OSA can worsen epilepsy, hypertension and cardiac failure; treatment of the sleep disturbance can improve the underlying condition, as demonstrated, for example, in the case of epilepsy.[17]
- A sleep disorder can be the presenting symptom or early warning sign of a number of neurological disorders. Increasingly, RBD is being seen as associated with a wide variety of neurological conditions,[18] and recognised as the harbinger (perhaps by many years) of some of them, such as Parkinson's disease and multiple system atrophy. Insomnia is an early feature of Morvan's syndrome and fatal familial insomnia. The same can be true of serious psychiatric illness, such as depression, mania and schizophrenia.
- Sleep loss or disruption can be a potentially serious complication of many types of medication used in general medicine, neurology and psychiatry.[5] Examples include some drugs used in the treatment of respiratory disease (theophylline), hypertension (beta blockers), Parkinson's disease (dopaminergic drugs) or depression (selective serotonin reuptake inhibitors).
- Particularly because of both public and professional unfamiliarity with the sleep disorders field, clinical manifestations of such disorders may well be misinterpreted as evidence of quite different disorders of a medical or psychiatric type. The consequence of such mistakes is, at best, delay in the correct diagnosis being made or, more seriously, the real diagnosis not being made at all.

The present review is concerned with this last fundamental link between sleep disorders and clinical practice in neurology, psychiatry and, indeed, other specialties. The diagnostic points made about the examples selected are based on evidence in the form of personal and published clinical experience, including the results of reports for which specific references are provided.

SLEEP DISTURBANCE IN GENERAL

Persistently not obtaining enough sleep, or having poor quality sleep because of frequent interruptions, or fragmentation by frequent subclinical arousals (as in OSA), is likely to cause tiredness, fatigue, irritability, poor concentration, impaired performance possibly causing injuries or accidents at work or while driving, or depression.[7] Of the various possible explanations for such changes in behaviour, sleep disturbance may well be overlooked, with failure to appreciate that, with an improvement in sleep (which is usually possible with the correct advice), such problems will be resolved. Occupational groups at special risk of sleep disturbance and its harmful effects include some clinicians.[19]

Excessive sleepiness, whatever its cause out of the many possibilities, including physical conditions,[20] is often misjudged as laziness, loss of interest, daydreaming, lack of motivation, depression, intellectual inadequacy, non-convulsive seizures or a number of other unwelcome states of mind. Sometimes, in very sleepy states, periods of ''automatic'' behaviour occur (ie, prolonged, complex and often inappropriate behaviour with impaired awareness of events and, therefore, amnesia for them). Such episodes can easily be misconstrued as reprehensible or dissociative behaviour, or prolonged seizure states. The paradoxical effect in young children of sleepiness causing overactivity has sometimes led to a diagnosis of attention deficit hyperactivity disorder inappropriately treated, as a result, with stimulant drugs instead of treatment for the sleep disorder.[21]

MISINTERPRETATION OF INDIVIDUAL SLEEP DISORDERS

The features of many individual sleep disorders are open to misinterpretations of a more specific nature. The following are examples of this, roughly in order of how often they occur in the general population. Details of sleep and its disorders, including treatment, are available elsewhere for professionals[22 23] or for patients and the general public.[24]

- Because of their sudden, surprising nature, *sleep starts* (invariably benign), consisting of a whole body jerk or intense sensory experience such as a loud bang or flash of light when going off to sleep (''the exploding head syndrome'').[25] The latter, in particular, may mistakenly be thought to suggest some serious disorder such as stroke or epilepsy.
- Reassurance is also appropriate about *isolated sleep paralysis*[26] (ie, other than that associated with narcolepsy). Surveys indicate that this condition, which occurs briefly when going to sleep or on waking up, is not uncommon but usually unreported unless it is frequent. It can generate much anxiety and, again, fear of having a stroke or other neurological problem.
- *Sleep related hallucinations*[27] (''hypnagogic'' when falling asleep; ''hypnopompic'' when waking up), occurring in various sensory modalities, are also common and can be frightening, especially to children. When combined with sleep paralysis, the experience can be so complicated and bizarre (including conversations with people or other beings, as well as feelings of threat and dread) that a psychotic process, especially of a schizophrenic nature, may well be suspected.[28]
- Parents of the many young children who bang their heads or roll about rhythmically at night may worry that this is a sign of an emotional problem or neurological disorder, particularly epilepsy. In fact, this *rhythmic movement disorder*[29] is benign and usually remits spontaneously by the age of 3–4 years, although occasionally it persists into adult life.

Abnormalities of the circadian sleep–wake cycle[30] provide further examples of the risk of misinterpretation.

- Over 20% of employees work shifts. Night shift workers, in particular, suffer from inadequate and poor quality sleep because they are required to work when their body clock is telling them that they should be asleep. As mentioned before, this *shift work disorder* is associated with various forms of ill health. The psychological effects of inadequate or poor quality sleep, compounded by the disruptive influence of shift work on family and social life, are commonplace in shift workers. These physical health issues and unfortunate psychosocial consequences can easily overshadow and distract from the true origins of the shift worker's primary problems. They are likely to lead to referral exclusively to medical or psychiatric services without advice about the underlying sleep disorder.
- The effects of *jet lag* are usually short lived but travellers who frequently cross several time zones on each flight can develop chronic sleep disturbances that can have serious effects on mood, performance and physical well being, the true cause of which may not be appreciated.

- Difficulty getting to sleep until very late and problems getting up in the morning, as well as daytime sleepiness and sleeping in late at weekends, characterise the *delayed sleep phase syndrome* (DSPS). These features are easily misinterpreted as awkward, lazy or irresponsible behaviour, or the usual form of school refusal, especially in adolescents in whom DSPS is common. In fact, where this sleep disorder does occur in adolescence it is the result of a combination of normal pubertal biological body clock changes (which shift the sleep phase later) and alterations in lifestyle involving staying up late for study or social reasons. The risk that the fundamental cause of the problem will not be recognised is increased if alcohol or hypnotic drugs are taken in an attempt to get to sleep, or stimulants to try to stay awake during the day.
- In the *advanced sleep phase syndrome*, which can be caused by normal body clock changes occurring in old age, there is a tendency to fall asleep in the evening (the opposite to the effect of body clock changes at puberty). This is likely to result in early morning waking when sleep requirements have been met. This should not be mistaken for the early morning waking associated with depression where the total amount of sleep is reduced.

As it is not generally realised how complicated behaviour can be during sleep, certain parasomnias are likely to be misinterpreted as other conditions.

- The common inherited conditions of sleepwalking and the related ''partial arousal disorders'' of sleep terrors and confusional arousals occur during non-REM sleep, mainly early in the night.[31] However dramatic and worrying to observers they might be, such conditions are usually temporary and not caused by medical or psychiatric factors which, however, can trigger episodes in those who are constitutionally predisposed.
- While *sleepwalking* may involve calm walking about in a semi-purposeful manner (although still with a risk of accidents), some sleepwalkers do much more complex things such as making themselves drinks or meals, following complicated routes outside the house or even driving a car.
- People with agitated sleepwalking or *sleep terrors* appear to be very fearful and distressed and rush about and cry out as if escaping from danger. Other sleepwalkers develop an eating disorder with excessive weight gain due to the amount of food they consume while they are still asleep at night. Yet others behave in an aggressive or destructive way causing injury to themselves or other people and, at times, sexual or other serious offences have been committed during a sleepwalking episode (and, indeed, some other sleep disorders).[32]
- Young children who have *confusional arousals* may well be thought by their parents to be ill in some way because of the degree of behavioural disturbance involved which is akin to that of sleep terrors.
- If it is not known that such complicated actions are compatible with still being asleep, it is likely to be assumed that the person was awake at the time and aware of what he or she was doing, and, therefore, responsible for what had happened. Alternatively, it might be claimed that the episodes are epileptic in nature or the result of some other physical or psychiatric state. Guidelines have been suggested for the recognition of sleepwalking automatisms, mainly for medicolegal purposes.[32]

The following conditions illustrate how, as mentioned earlier, the true nature of sleep disorders characterised by excessive daytime sleepiness may well be misconstrued.

- *OSA*,[33] which affects about 4% of men and at least 2% of women, can cause excessive sleepiness, changes in personality and adverse effects on social life and performance at work, as well as intellectual deterioration to the extent that dementia is suspected. Only about one-tenth of those with OSA seek medical advice, probably because many of the others do not realise that their daytime problems are the result of their often severely disrupted sleep. Those who have sought medical advice may well have been treated initially, before their sleep disorder was recognised, for the complications of their OSA (such as hypertension or depression) rather than the OSA itself.[34] Clearly, early recognition of this treatable condition is highly desirable. The same is true of OSA in children (generally affecting about 2%). The usual cause at this age is enlarged tonsils and adenoids the removal of which can improve their sleep and, as a result, at least lessen any learning and behaviour problems which, otherwise, are likely to have been attributed to the other, more usual causes.[35] OSA, usually of more varied origins, complicates many forms of learning disability.[6]
- *Narcolepsy*,[36] characterised mainly by sleep attacks, as well as more general sleepiness, is not the rarity once supposed. Its prevalence in Western societies is in the order of 0.02–0.05%, which is only somewhat less than Parkinson's disease or multiple sclerosis. When (as is usual) cataplexy, with recurrent loss of tone causing collapse or weakness of one part of the body or another, usually in response to strong emotion, is also present, there is even more scope for mistakes. Cataplexy can be misconstrued as syncope, epilepsy or attention seeking behaviour. Other possible components of the narcolepsy syndrome (ie, hallucinations, which can be especially vivid, and sleep paralysis) as well as associated automatic behaviour can also be misinterpreted. It has been reported that, in the year prior to the diagnosis being definitively made at a sleep disorders centre, narcolepsy had been considered in only 38% of cases.[37] The incorrect diagnoses had included other neurological disorders such as epilepsy and a variety of psychiatric problems, especially neurosis and depression. Neurologists had made the correct diagnosis in 55% of the cases they had seen, internists in 23.5%, general practitioners in 21.9% and psychiatrists in 11%. Paediatricians had failed to recognise the condition as narcolepsy in all the children they had seen, possibly because of the special difficulties that can be encountered in recognising the condition at an early age,[38] but also because it is not generally realised that the onset of narcolepsy occurs before adulthood in at least a third of cases. Hypothyroidism and hypoglycaemia are other possible misdiagnoses of narcolepsy.

A number of other sleep disorders, although individually not particularly common, are also at risk of not being correctly recognised, with potentially serious consequences.

- In *RBD*,[39] muscle tone is pathologically retained during REM sleep, allowing dreams to be acted out (most dreaming occurs during REM sleep). Violent dreams are likely to cause injury to the patient or bed partner. As mentioned earlier, RBD has many causes or associated conditions, including a strong association with neurodegenerative disorders such as Lewy body disease, multiple system atrophy, Parkinson's disease and also with narcolepsy. There is also a link with some forms of medication, including antidepressants. Although mainly described in elderly males, it has also been reported at other ages, including children, and in women. The condition (which is eminently treatable, even in the presence of neurodegenerative disease) may well be confused with other dramatic parasomnias such as sleep terrors,

nocturnal epilepsy or panic attacks, despite their different distinctive features. Especially if the bed partner is attacked, a psychological motive may be suspected.

- A number of non-convulsive types of epilepsy are closely related to sleep, including benign centro-temporal epilepsy, benign partial epilepsy with affective symptoms, benign occipital epilepsy and also *nocturnal frontal lobe epilepsy* (NFLE). All can give rise to dramatic behaviour which is easily construed as some other type of night-time disturbance. This is particularly so in NFLE, which occurs in both adults[40] and children.[41] In this form of epilepsy, seizures can consist of such movements as kicking, hitting or thrashing, and vocalisations which include screaming, shouting and roaring. These and the other possible manifestations are at serious risk of being misdiagnosed (especially because even ictal EEGs can be unremarkable) as other dramatic events such as sleep terrors or pseudoseizures. The brief and often frequently occurring forms of NFLE may simply be viewed as restless sleep. Informed clinical enquiry can be valuable in reaching the correct diagnosis.[42]
- The episodic, prolonged sleepiness in the *Kleine–Levin syndrome*,[43] accompanied by often bizarre and out of character behaviour when the patient is awake, understandably causes confusion in the minds of those who are unfamiliar with the condition. Some people with this disorder have initially been thought to perhaps have encephalitis, cerebral tumour, epilepsy, drug addiction or a psychiatric problem.[44]

It is important to acknowledge that a patient may have a combination of sleep disorder and other conditions of a different nature (and, indeed, more than one type of sleep disorder), especially in the elderly. Therefore, it is all the more important that each complaint and its cause, including the possibility of sleep disorder, are assessed thoroughly. Without this, there is a serious risk that the wrong conclusion will be reached, perhaps causing unnecessary concern but also denying the patient the correct treatment for the sleep disorder which, if properly implemented, is likely to be effective.

SLEEP HISTORY

The following outline illustrates the main clinical enquiries that should supplement usual history taking schedules. A more detailed account is provided elsewhere[45]; a modified approach is required in the case of children and adolescents.[46]

Three basic screening questions for any patient are

- Do you have any difficulty getting off to sleep or staying asleep?
- Are you very sleepy during the day?
- Do you have any disturbed episodes at night?

The patient's bed partner or other relative should also be questioned.

Positive answers call for a detailed sleep history, essential elements of which are:

- the precise nature of the sleep complaint, its onset and development;
- medical or psychological factors at the start of the sleep problem or which might be maintaining it;
- patterns of occurrence of the sleep problem, including provoking or ameliorating factors, and differences in sleep patterns between weekdays and weekends;
- the sleeping environment, regularity of sleep habits and other aspects of ''sleep hygiene'' (ie, practices that are conducive to sleep[47]);
- effects on mood, work, social life and other family members;
- effects of past and present treatments for the sleep problem, and medications taken now or in the past for other conditions;
- details of the patient's typical 24 hour sleep–wake pattern, starting with evening events leading up to bedtime, time and process of getting to sleep, events during the night, time and ease of waking up, daytime sleepiness (including naps), as well as mental state and behaviour during the day;
- estimation of the duration and soundness of overnight sleep;
- features of particular diagnostic importance such as a combination of obesity, loud snoring or snorting and apnoeic episodes (OSA), wide discrepancy between weekday and weekend sleep patterns (DSPS), sleep attacks and cataplexy (narcolepsy), repeated jerking at night (periodic limb movements in sleep) or violent dreams and behaviour during sleep (RBD).

A screening questionnaire for use with adults[48] or younger patients[49] can be a useful starting point in assessment. A structured sleep diary, recording day and night events over 1–2 weeks, may also reveal further valuable information. Other potentially relevant details may be contained in the patient's medical, psychiatric and social histories, including occupational factors and also habits (such as caffeine, alcohol or nicotine consumption and use of illicit drugs) which might affect sleep. A family history of sleep disorders might also be revealing.

These enquiries should be accompanied by a review of systems, as well as physical and mental state examination. It is important to identify any neurological, general medical or psychiatric disorder likely to affect sleep, or physical anomalies of possible importance such as those which predispose to OSA, especially obesity and nasopharyngeal abnormalities.

Clinical information from these sources may well be sufficient to at least provisionally formulate the problem correctly. In a proportion of cases, special investigations will be required, or referral to a sleep disorders service.

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