

## ADHD and Sleep problems

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### Abstract

Sleep is a vital process not only for survival but also to maintain physical and psychological health. ADHD is often associated with sleep difficulties. A reduction in sleep quality and duration can lead to significant behavioural and psychological manifestations. A comprehensive assessment should be carried out, involving a detailed sleep history, sleep diary, evaluation of any associated primary sleep disorders and an assessment of the role of ADHD medication. Management is 'diagnostically driven' and should include sleep hygiene with behaviour interventions, treating other comorbid conditions, optimising ADHD treatment and, if necessary, short-term use of sleep medication.

### Introduction

#### Sleep anatomy and physiology.

Although there has been a significant increase in our knowledge over the past few decades regarding the underlying mechanisms which control sleep, its basic function remains unclear. Adequate sleep does, however, appear to represent a "biological imperative", vital for the maintenance of optimal physical and psychological wellbeing and survival (1-5).

Sleep and wakefulness are normally regulated by coupled homeostatic ("Process S") and circadian ("Process C") mechanisms, summarised in Table 1

| Process                                  | Function                                                              | Putative Mechanism                                                                                                                                                                                      |
|------------------------------------------|-----------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Homeostatic, -<br>"Process S"            | Influences depth and length of Sleep and "Sleep Drive"                | Progressive accumulation of brain metabolites, -e.g. cytokines, adenosine, resulting in an inescapable "sleep debt"                                                                                     |
| Endogenous Circadian Rhythm, "Process C" | Influences timing and duration of sleepiness versus daytime alertness | Circadian "clock" in supra-chiasmatic nucleus, - influenced and to a certain extent "entrained" by light dark exposure; also by "clock genes", resulting in morning "lark" and night "owl" individuals. |

Table 1 Coupled Mechanisms for Sleep regulation (3,5,6)

## Normal Sleep Characteristics in Childhood and Adolescence

From an average of around 16 -18 hours at term, sleep duration reduces over childhood to between 7 to 8 hours in late adolescence (see Table 2).

Across childhood and adolescence, according to limited data available, the time taken to fall asleep ("sleep onset latency") averages between 15 to 20 minutes, and does not appear to show much variation depending on age.

| Age              | Average Sleep duration (hours) |
|------------------|--------------------------------|
| Full Term        | 16-18                          |
| 1 year           | 15                             |
| 2 years          | 13-14                          |
| 10 years         | 8-10                           |
| Mid Adolescence  | 8½                             |
| Late Adolescence | 7-8                            |

**Table 2 Average Sleep Duration at Different Ages (2,3,7,8).**

### Consequences of disordered sleep

Reduction in the duration and quality of sleep results in a number of daytime manifestations affecting cognitive function and behaviour alongside the familiar symptoms of sleepiness, fatigue, yawning etc., associated with "sleep debt". Reduced alertness may be accompanied by noticeable hyperactivity, impulsivity, and inattention - the core symptoms observed in ADHD. A synopsis of potential signs and symptoms which may be observed as a consequence of disordered sleep is listed in Table 3. It is important to keep in mind the potential for family disruption and discord to which these symptoms may contribute, as well as possible implications of disturbed parental and sibling sleep (1,2,3,17,18).

|                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                   |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>• Drowsy, fatigued, yawning, rubbing eyes</li> <li>• Reduced alertness, falling asleep</li> <li>• Reduced sleep latency (time to fall asleep) on Multiple sleep latency test</li> <li>• Increase hyperactivity, impulsivity and inattention</li> <li>• Reduced cognitive flexibility</li> </ul> | <ul style="list-style-type: none"> <li>• Reduced verbal creativity</li> <li>• Poor abstract reasoning</li> <li>• Impaired motor skills</li> <li>• Memory impairments</li> <li>• Increased mood lability and aggression</li> </ul> |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

**Table 3. Behavioural and Psychological manifestations of Disordered Sleep(2,3,9-16,)**

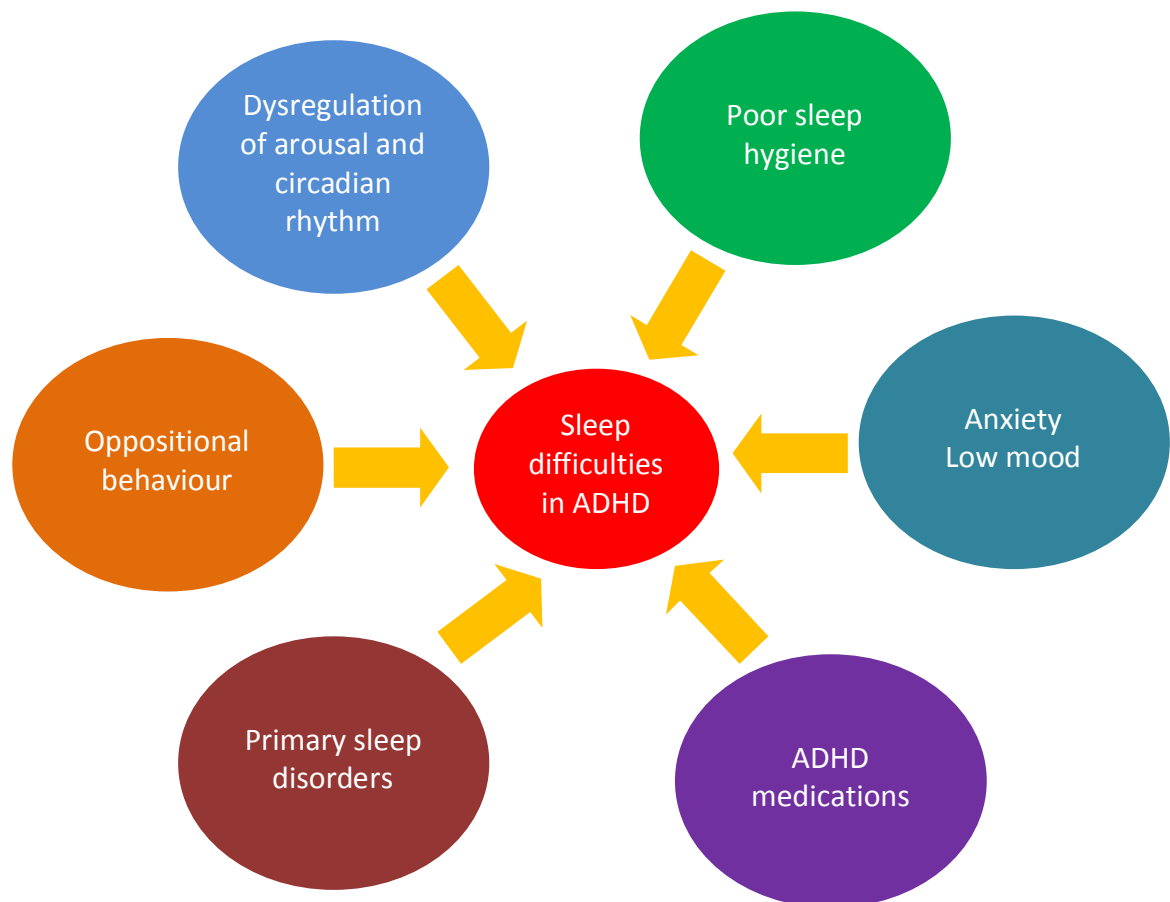
## Sleep and ADHD

A clear association between disordered sleep and ADHD is well established, with a reported prevalence that approaches 50% or more (compared to for example 11% of normal 4-12 yr old children) comprising a range of self-reported and parent-reported difficulties, which include bedtime resistance, increased sleep latency and sleep of poor quality (e.g. with frequent waking) or duration (19,20). The poor concordance between parental accounts and objective measures such as polysomnography and actigraphy is likely to be explained by night-to-night variability in sleep patterns and methodological difficulties such as the challenge of reproducing a "naturalistic" sleep environment in a sleep laboratory setting.

Impaired sleep may result in psychological and behavioural problems identical to those seen in ADHD. Sleep difficulty can not only therefore mimic ADHD but can also potentially cause exacerbation of ADHD symptoms. This can add further to the burden of care within families, such as reported excessive parental tiredness, irritability, social withdrawal, arguments, and time off work, all seriously affecting quality of life.(21,22)

Factors which may contribute to sleep difficulties in children and young people with ADHD (see figure 1).

The aetiology of sleep difficulties in ADHD is complex and not well studied or understood; more than one cause may be implicated in any individual.



**Figure 1. Contributing factors to sleep difficulties in ADHD**

## Primary Sleep Disorders

A “Primary” sleep disorder may result in reduced daytime alertness and daytime ADHD symptoms due to, for example, reduced sleep duration and/or fragmented sleep. Important examples include obstructed breathing and sleep apnoea, restless legs syndrome/periodic leg movement disorder, narcolepsy/cataplexy, and delayed sleep phase syndrome of adolescence. Recognition and specific treatment of these albeit relatively uncommon disorders can be effective and lead to reduced ADHD symptoms. A brief synopsis is in Table 4.

| “Primary Sleep Disorder”                                             | Comments                                                                                                                                                                                                                                                              |
|----------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Obstructive Sleep Apnoea/<br>Hypopnea Syndrome<br>(OSAHS) (19,23-27) | Assess for obesity and adenotonsillar hypertrophy.<br>Noisy breathing at night; adenoidal facies; “mouth breathing”<br>ADHD symptoms may be remediable by ENT surgery                                                                                                 |
| Restless Legs Syndrome/<br>Periodic Leg movement Disorder<br>(28-31) | Fidgety, on the move, - “growing pains” in extremities.<br>Poor sleep and movements worse when settling at night.<br>Association with caffeine use and low serum ferritin.<br>Increasingly acknowledged as a treatable extrapyramidal disorder, overlapping with ADHD |
| Narcolepsy/Cataplexy (32)                                            | Rare. Cataplexy results in episodes of collapse from rapid change in emotion. Disrupted sleep with hypnagogic hallucinations, sleep paralysis and daytime sleepiness, naps, and ADHD symptoms                                                                         |
| Delayed Sleep Phase Syndrome<br>(33-35)                              | Up to 3% adolescents. Sleep late, wake late if allowed, but pressured to attend school, college etc.<br>Challenging to treat (attempt to recalibrate sleep-wake cycle)                                                                                                |

**Table 4 Examples of “Primary” Sleep Disorders which may overlap with or mimic ADHD**

## Behavioural Disruption and Sleep Difficulties in ADHD

Sleep disruption, particularly bedtime resistance and increased sleep latency in ADHD, frequently result from inappropriate and inconsistent parental limit setting combined with oppositional behaviour, exacerbated by poor “sleep hygiene” (i.e. poor control of behavioural and/or environmental factors that can interfere with sleep, including lack of bedtime routine). However, before assuming that in individual cases such sleep difficulties are “behavioural” or environmental, it is important to keep in mind that ADHD-associated CNS dysregulation of arousal and circadian rhythms may be contributory factors (3,36), - not so much a question of “won’t sleep”, but “can’t sleep”.

## Internalising Disorders and Autism affecting Sleep in ADHD

Anxiety and depression are well recognised “comorbid” accompaniments of ADHD in many children and young people. Early recognition and screening for these conditions is part of the clinician’s ongoing responsibility, whilst recognising that sleep disruption, with attendant daytime sequelae may result (3, 37). Anxiety is also more likely to be observed in children who lack a capacity for “self-soothing” as part of normal maturation, and in those identified as exhibiting problems such as impaired sensory integration. Similarly children and young people who have autism spectrum disorder with ADHD demonstrate a high rate of potentially refractory sleep difficulties, which correlate positively with the severity of the daytime behavioural problems and communication impairments (2,3,38,39).

## Daytime environmental exposures and Sleep problems in ADHD

Overstimulation and excessive exercise close to normal sleep times may contribute to difficulties settling at night; the importance of good sleep routines and environment cannot be understated. Exposure to caffeine-containing drinks and beverages may promote wakefulness and arousal. Specific medications, particularly neurostimulants may also be implicated. Psychostimulants have a potential to increase sleep latency, particularly when administered later in the day or as an extended-release preparation. Although convincing objective research evidence for a link between stimulant medication and disrupted sleep is scanty, it is clear that this is a common clinical problem. (40-42). Other prescribed medications which can impair sleep include antiepileptic drugs (rarely) and antidepressants (3).

## Assessing Sleep in ADHD

Assessment is based on appropriate enquiry about sleep routines and evening activities, (including food, beverages, medication), sleep environment, time to get into bed, time to settle to sleep, and the quality and duration of sleep. Any alteration in daytime behaviour or any change in sleep pattern coinciding with medication initiation or modification should also be noted. This information can be captured by self-report, and parental report (2, 3), and ideally by completion of widely available sleep diaries. Systematic evaluation is possible using specific questionnaires (43,44). When relevant, other assessments such as upper-airway assessment for tonsillar or adenoidal obstruction may be required, or when suspecting restless legs syndrome/PLMD, blood assay for ferritin level (30,31). Considering the potential causes of disrupted sleep, careful assessment to detect associated anxiety, low mood, and autism spectrum disorder should not be overlooked.

If a primary sleep disorder is suspected from the history, a referral to a specialist sleep centre for further investigation such as polysomnography/actigraphy is indicated.

## Management of Sleep Disorders in ADHD

Management is “diagnostically driven”, and depends on thorough assessment and a formulation to include the likely underlying cause or causes.

## Primary sleep disorders

Specific individual management strategies are summarised in Table 5.

| Primary Sleep Disorder                                        | Management Strategies                                                                                                                   |
|---------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| Obstructive sleep apnoea/hypopnoea syndrome (OSAHS)           | Weight reduction; adenotonsillectomy. (25-27)                                                                                           |
| Restless legs Syndrome/periodic limb movement disorder (PLMD) | Oral Iron; avoid caffeine.<br>Dopaminergic agents e.g. Sinemet. Pramipexole. Clonidine.<br>Opiates such as codeine. Gabapentin. (29,30) |
| Narcolepsy/cataplexy                                          | Psychostimulants; SSRIs; sodium oxybate. (32)                                                                                           |
| Delayed Sleep Phase Syndrome of adolescence                   | “Chronotherapy” (re-adjusting sleep/wake cycle).<br>Melatonin. Light therapy. (33,34)                                                   |

**Table 5. Management of Primary Sleep Disorders**

## Management of Primary Sleep Disorders

Psychological/Behavioural Causes and adverse environmental triggers and exposures should be managed in the first instance by well-established strategies, summarised in table 6. It is particularly important not to overlook the potential contribution of anxiety and altered mood to sleep difficulties and specific enquiry should be made about any potential triggers. It is particularly important to assess so-called “sleep hygiene” (see earlier) in this era of multimedia with the plethora of potentially stimulating (and light emanating) devices. These should be strategically and progressively removed from the bedroom environment.

| Behavioural Methodology examples                                   | “Sleep Hygiene” issues                                           |
|--------------------------------------------------------------------|------------------------------------------------------------------|
| Consistent limit setting                                           | Regular scheduling                                               |
| Positive (e.g. token) reinforcement                                | Appropriate bed time                                             |
| Reduce anxiety ; relaxation training/tapes                         | Bedtime preparation routines                                     |
| Avoid negative associations (e.g. bedroom seen as punishment zone) | Relationship to meals, exercise, caffeine, stimulating activity. |
| Individual CBT in older children and adolescents                   | Ambient noise, temperature, light, DVD, Playstation, X-Box etc.  |

**Table 6. Psychological and Behavioural Strategies for Disordered Sleep in ADHD (2,3)**

As noted earlier, the use of psychostimulants for control of daytime ADHD symptoms may cause or exacerbate insomnia. Treatment options when faced with sleep difficulties which may be medication related, include stimulant dose reduction, switching to a shorter acting neurostimulant, or in refractory cases discontinuing the medication completely (13,28,45). If the sleep disturbance continues, it may be worth undertaking a brief pragmatic trial of short-acting methylphenidate in the evening, about an hour before the time that the child should be asleep; this is effective in a subgroup of children with ADHD (46), probably those in whom the symptoms of this condition are keeping them awake at night. The usual convention is a trial of half of one of the daily doses, i.e. if the child was taking 20 mg three times daily then a dose of 10 mg would be given in the evening. This need only be tried for one or two nights. If the sleep is improved, it may be continued but if the sleep is worse or unchanged the evening methylphenidate dose should be stopped. If stimulant medication causes a deterioration in sleep, atomoxetine, which is not associated with sleep disruption (47), should be considered as an alternative.

### Medications for sleep promotion in ADHD-Associated Insomnia.

The use of medication for disrupted sleep in ADHD is rarely the first and only choice; it should be combined with behavioural strategies aiming to sustain improvement and minimise adverse effects. There are no licensed medications for sleep promotion in children and adolescence and indeed the research base is sparse. Prescribing must be initiated on a “named patient”, off-label basis, under “specialist” supervision (See British National Formulary for Children (BNFC) for support and guidance). There is little guidance in the paediatric and psychiatric literature, although recent reviews may be useful (13,28,45,49,50). Prescribing needs to take into account a risk-benefit analysis for the individual patient and medication.

In the UK medications listed for consideration, but not “recommended”, by the BNFC, for “occasional” and /or “short-term” use include chloral derivatives, the antihistamine promethazine (“Phenergan”), and melatonin. Clinicians will need to assess the risks and benefits of longer-term treatment on an individual basis; children may revert to a pattern of poor sleep when sleep medications are withdrawn or inadvertently overlooked.

**Melatonin (MLT)**, in both immediate and extended-release forms, is widely prescribed, in “pharmaceutical quality” preparations in the UK. Evidence for the efficacy of MLT for sleep promotion

is based mainly on open studies and case reviews, although a small number of randomised trials have been published (51,52,53 ). In practice, adverse effects with MLT are relatively uncommon and self-limiting. There is increasingly reassuring evidence that this is a safe medication in hypnotic doses of up to 10mg (54,55). In such doses, administration is recommended 30 minutes before sleep time, and the half-life is short with no likely hangover or morning-after ill effects. Long-term safety of MLT has not been convincingly established and there are some residual questions, including potential adverse endocrine and immunological effects. The effectiveness of MLT may be limited by its short half life (1-2hrs) and rapid elimination in which case an extended-release preparation may be considered. Future potential therapeutic alternatives with longer half-life properties include MLT analogues such as Ramelteon, Tasimelteon, and Agomelatine (48).

Though still in use by some clinicians, there is no evidence base to support the use of **Chloral Hydrate**. Effectiveness may be limited by gastrointestinal intolerance and sometimes daytime dizziness reflecting the long longer half-life of the main active metabolite trichlorethanol. Cautious short-term use may be justified in treatment-refractory patients

A wide range of Antihistamines are employed empirically for sleep promotion in children, particularly in primary care. For example, as noted earlier, the BNFC supports lists promethazine (Phenergan) for short-term use; daytime drowsiness, gastrointestinal upset, paradoxical excitation and tolerance may limit effectiveness (56,57).

**Clonidine Hydrochloride**, a central alpha-2 adrenergic agonist is widely used for sleep promotion in childhood practice in the USA, often in higher doses than would usually be considered in the UK. Onset of action is rapid with peak effects within 2 to 4 hours. Evidence for efficacy from clinical trials is limited and potential adverse effects include postural hypotension, syncope, dry mouth and fatigue (58,59).

The use of **Benzodiazepines** for insomnia in ADHD is not supported because of significant limitations and adverse effects, including the risk of exacerbating hyperkinesia. Shorter acting **Non-Benzodiazepine Receptor Agonists** or “Z Drugs” such as **Zolpidem**, **Zopiclone** are popular hypnotics in adult practice and may have a limited role in refractory insomnia in ADHD. Potential adverse effects which may limit usefulness include dizziness, headache and hallucinations (60). In the USA **Atypical Antidepressants (5-HT Antagonist)** such as Trazodone and Mirtazapine are sometimes prescribed for sleep promotion (61,62), although there is little experience with these agents in the UK and no evidence base to support use.

There is no “ideal” hypnotic medication for use in refractory insomnia in ADHD. Pragmatically, ideally short-term prescribing is perhaps worthy of consideration in individual circumstances. Melatonin appears to be the medication associated with the fewest adverse effects but it is not always effective or may appear to lose its effect over time. Whatever medication is tried, periodic breaks from treatment are prudent to assess whether ongoing treatment is necessary. Most hypnotics will remain ineffective in the presence of poor sleep routines, overstimulation at bedtime or the challenges of nocturnal multimedia.

## Key Points

- Sleep difficulties are highly prevalent in ADHD, are often multifactorial in origin, and significantly impair quality of life for the child and family.
- Sleep deprivation can produce symptoms that mimic ADHD.
- Sleep difficulties exacerbate daytime ADHD symptoms.
- Shared biological dysregulation in ADHD may contribute to disordered sleep.
- Assessment of ADHD is incomplete without a sleep history.
- Sleep diaries are particularly useful in assessment.

- In assessment “Primary Sleep Disorders” (Obstructive Sleep apnoea, Restless leg Syndrome/Periodic leg movement Disorder, Narcolepsy/Cataplexy, Delayed Sleep Phase Syndrome), though rare, need consideration; referral to a sleep specialist may be indicated .
- Behavioural disorders, internalising disorders and autism spectrum disorder should be considered/ excluded in assessment
- Daytime medication such as neurostimulants may cause/exacerbate sleep problems in ADHD.
- Management is “diagnostically driven”; it should always include behavioural intervention and consideration of sleep routines and environment.
- Medication (hypnotics) and manipulation of daytime ADHD medications may be used on an individual basis to promote and improve sleep.
- If medication is prescribed for sleep in childhood and adolescence this is necessarily “off-label”, ideally short term, and on a named-patient basis under specialist supervision and surveillance.

## GP Comment.

### What have I learned from this paper?

1. Disordered sleep is much more common in children with ADHD; self-report and parent-report assessments have suggested a prevalence approaching 50%.
2. Insufficient sleep (“sleep debt”) can result in hyperactivity, impulsivity and inattention, the same core symptoms that are seen in ADHD. In addition, it may contribute to family disruption, adding to family stress and behavioural problems. Treating the sleep problems successfully can resolve the ADHD symptoms in some cases.
3. Sleep disturbance can not only mimic ADHD but can also exacerbate the symptoms in children with established ADHD.
4. Although good “sleep hygiene”, (involving control of behavioural and environmental factors that can interfere with sleep), is important, some children with ADHD have underlying sleep problems that will not resolve with these measures alone.
5. The management of sleep problems in ADHD depends on the underlying diagnosis: obstructive sleep apnoea/hypopnoea, restless legs syndrome, periodic limb movement disorder, narcolepsy and delayed sleep-phase syndrome of adolescence of all require specific management strategies.
6. Medication for ADHD can either worsen or improve sleep; this depends not only on the type of medication but also the characteristics of the individual.
7. There are no licensed medications for treating sleep problems in children with ADHD but melatonin is widely used to decrease time to sleep onset (sleep latency). It may not be very effective in maintaining sleep throughout the night, however.
8. Clonidine can be helpful both in treating ADHD symptoms and in promoting sleep.

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