



Identifying and managing sleep disorders associated with ADHD

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Practice points

- Sleep disturbances are associated with ADHD in as many as 70% of patients.
- Both subjective (i.e., detected with questionnaires) and objective (i.e., revealed by neurophysiologic tools) sleep alterations have been found to be significantly more frequent in individuals with ADHD compared with controls.
- Behavioral problems (e.g., limit-setting disorder), as well as delayed sleep-phase disorder, restless legs syndrome, sleep-disordered breathing and the effect of psychiatric comorbidity may contribute to sleep complaints in patients with ADHD.
- Clinicians should screen for sleep disturbances at each visit with ADHD patients.
- Polysomnography and other objective measures are indicated only in selected cases (i.e., suspicion of sleep-disordered breathing or other causes of sleep fragmentation, such as nocturnal seizures).
- There is a paucity of empirical evidence to guide treatment of sleep disturbances in ADHD. Behavioral interventions remain a mainstay of treatment for many sleep problems, although clinical trials are needed to confirm their efficacy and refine protocols. As for pharmacological treatment, the largest and best available evidence supports the effectiveness and good tolerability of melatonin for sleep-onset delay.

SUMMARY Although often overlooked, sleep disturbances are frequent in ADHD, affecting a sizable proportion of patients. Sleep complaints in patients with ADHD may be due to behavioral factors (e.g., limit-setting disorder), as well as objective alterations, such as delayed sleep-phase disorder, restless legs syndrome, sleep-disordered breathing and the effect of stimulants or associated comorbid disorders. We suggest to systematically screen for sleep disturbances at each visit by means of subjective tools (i.e., questionnaires and sleep

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diaries) and, when indicated, objective measures (i.e., polysomnography, actigraphy and the multiple sleep latency test). Empirical evidence for the treatment of sleep disturbances associated with ADHD is limited. Besides initial studies on behavioral interventions, the largest and best available evidence demonstrates the effectiveness and good tolerability of melatonin for sleep-onset delay. Further randomized controlled trials of pharmacological and nonpharmacological interventions are needed.

ADHD is a common childhood-onset psychiatric condition characterized, according to the DSM-IV-TR criteria [1], by impairing and pervasive core symptoms of inattention and/or hyperactivity–impulsivity, which persist into adulthood in up to 65% of cases [2].

The association between ADHD and other psychiatric or neurodevelopmental conditions, such as oppositional defiant disorder, conduct disorder and mood/anxiety disorders, has been well studied [3]. Conversely, the relationship between ADHD and sleep disturbances has been largely overlooked, both from a research standpoint and in clinical practice. This is reflected by the lack of specific recommendations on sleep assessment in the guidelines and practice parameters on ADHD in the last decade [4,5]. Indeed, when asked, parents of children with ADHD do report sleep problems in their children in a sizable portion of cases. According to Corkum *et al.*, parents report sleep problems in 25–50% of children with ADHD compared with 7% of normal controls [6]. In addition, considering mild (besides severe) sleep alterations, a recent study showed that more than 70% of children with ADHD present sleep impairment [7].

Fortunately, in the past years there has been an increasing interest in sleep problems associated with ADHD, as proven by the inclusion of sleep evaluation in recent ADHD guidelines and consensus statements, both in children [8] and in adults [9]. Sleep issues in patients showing potential ADHD symptoms is of particular relevance for three reasons [10]:

- Sleep disturbances may represent a significant source of distress for the child and/or the family;
- Sleep problems may worsen ADHD symptoms, as well as associated mood and emotional disorders;
- Quantitative or qualitative alterations of sleep may cause problems with mood, attention and behavior, thus sleep disturbances may mimic ADHD symptoms in children misdiagnosed with ADHD.

Therefore, symptoms of inattention, hyperactivity and/or impulsivity may be improved or even eliminated with treatment of the primary sleep disorder.

In this paper, addressed mainly to clinicians, we provide an overview of the main sleep disturbances/disorders associated with ADHD, their diagnostic assessment and available therapeutic options. We will base our therapeutic recommendations on existing empirical evidence, integrating it with our clinical experience when no empirical data are available. We refer to both studies in children and adults. Since most of the research in the field has been carried out in childhood, this paper mainly focuses on the identification and management of sleep problems in children.

Sleep disturbances & disorders associated with ADHD

Sleep can be studied by means of so-called ‘subjective methods’, in other words clinical interviews or questionnaires filled out by the patient (i.e., in pediatric settings, by the parents or, less frequently, by the children themselves) and ‘objective methods’, in other words by means of neurophysiological tools such as polysomnography (PSG), actigraphy, infrared video analysis and the multiple sleep latency test. A more comprehensive classification of sleep disorders can be found in the International Classification of Sleep Disorders (Second Edition) [11] and, specifically for children, in the paper by Owens and Mindell [12]. **Table 1** provides a concise description of these neurophysiological diagnostic procedures, while **Table 2** reports the main subjective and objective parameters that can be derived from sleep studies. Several subjective (e.g., [13–15]) as well as objective sleep studies (e.g., [16,17]) have been conducted in ADHD. It is impractical to mention and discuss all these studies here. Fortunately, evidence from meta-analyses (in children but not in adults) that allow a quantitative overview after pooling all pertinent studies is available. In the most recent meta-analysis on ADHD and sleep in children, Cortese *et al.* found evidence supporting that children with ADHD present with

Table 1. Objective tools to assess sleep and sleep disturbances.

Technique	Description	Useful for the diagnosis of
PSG	Recording during sleep of physiologic parameters including: ▪ Brain electrical activity ▪ Eye and jaw muscle movement ▪ Leg muscle movement ▪ Airflow ▪ Chest and abdominal excursion ▪ Oxygen saturation ▪ ECG	SDB disorders Sleep-related movement disorders Hypersomnolence of unknown origin
Actigraphy	Monitoring cycles of physical activity and rest by means of an actimetry, a wrist-watch-like device (put on the wrist or ankle) that continually records movements. The data are analyzed offline. Sleep parameters (sleep–wake periods, total duration of sleep, number of arousals and length of sleep onset) are inferred by the patterns of rest/movement	Delayed sleep-phase disorder
Multiple sleep latency test	Four or five 20–30 min nap opportunities given at 2 h intervals during the day. The basic parameters measured are latency to sleep onset and latency to REM sleep on the polysomnographic recording. Multiple sleep latency test provides a measure of an individual's level of daytime sleepiness	Narcolepsy
Infrared video camera	To monitor body movements during sleep in a dark environment	Abnormal behaviors or movements during sleep

PSG: Polysomnography; REM: Rapid eye movement; SDB: Sleep-disordered breathing.

significantly more sleep problems than controls as reported by parents, including bedtime resistance, sleep-onset difficulties, night awakenings, difficulties with morning awakenings, sleep-disordered breathing (SDB) and daytime sleepiness [18]. They also found that children with ADHD are significantly more compromised compared with control subjects in several parameters from objective studies, such as sleep-onset latency (on actigraphy), the number of stage shifts/h of sleep, the apnea–hypopnea index, sleep efficiency on PSG, true sleep time on actigraphy and average time to fall asleep for the multiple sleep latency test (indicating that children with ADHD have higher levels of daytime sleepiness than controls). Of note, excluded studies assessing subjects pharmacologically treated or with comorbid anxiety/depressive disorders were excluded from the meta-analysis, thus suggesting that the significant differences in sleep parameters (both subjective and objective) are not accounted for exclusively by ADHD drugs or psychiatric comorbidities, although these factors may and do impact sleep in children with ADHD. Clinical experience suggests that a sizable part of sleep problems, especially those manifesting with bedtime resistance, may be accounted for by inappropriate limits set by parents and dysfunctional interactions between parents and

children, leading to inappropriate sleep hygiene or oppositional behaviors. This represents a common condition in our experience, especially when ADHD children present with comorbid oppositional defiant disorder. Other behavioral sleep problems are common in children with ADHD, including sleep-onset associations and nighttime anxiety. However, studies in recent years (summarized in [10]) increasingly show that, besides behavioral dysfunctional patterns between parents and children, individuals with ADHD present with objective neurobiological alterations, which may impact sleep. Three of these, discussed in the following subsections, are of particular relevance.

■ Delayed sleep-phase disorder

There is preliminary but increasing evidence demonstrating that a subset of individuals with ADHD may present with a delayed evening increase in endogenous melatonin levels, both in children [19] and in adults [20]. Since melatonin is involved in the regulation of sleep–wake patterns, its dysregulated secretion may lead to a delayed sleep-phase disorder, in other words, disruption of sleep–wake patterns that manifest with an anticipation or delay in sleep phase so that the patient finds it difficult to fall asleep at a ‘conventional’ time in the night. This is

Table 2. Sleep parameters from subjective and objective studies.

Parameter	Description	Means of assessment
Subjective parameters		
BR	Behaviors such as the child refusing to get ready for bed, refusing to remain in the bed or requiring a parent to be present at bedtime. It is included in the nosographic entity 'limit-setting sleep disorders'. It is often the result of parental difficulties in setting limits and managing behavior	Parent questionnaires or direct unstructured interview
SOD	Difficulty with falling asleep (within 20 min after going to bed according to some authors). Factors that may contribute to SOD include: psychopathologies (e.g., mood disorders), inappropriate sleep hygiene or objective sleep disorders (e.g., RLS)	Parent/child questionnaires; sleep diaries
NA	May require parental intervention for the child to return to sleep. They are often related to inappropriate sleep-onset associations (conditions that the child learns to need in order to fall back to sleep), such as when a child presents with bedtime sleep-onset associations that are not readily available during the night (e.g., having parental presence)	Parent questionnaires; sleep diaries
SD	Duration of total sleep, as perceived by the parent or the child. SD is defined as time asleep at night, or as time asleep plus in bed awake at night or as total time asleep across 24 h	Sleep diaries
DMA	Behaviors such as the child refusing to wake up by himself or having difficulty getting out of bed in the morning. It may be the consequence of inadequate sleep or the result of parental difficulties in setting limits and managing behavior	Parent/child questionnaires
DS	Persistent tiredness and lack of energy with a tendency to fall asleep. Causes of daytime sleepiness include chronic sleep deprivation, underlying sleep disrupters (e.g., obstructive sleep apnea, RLS and periodic limb movements in sleep), psychiatric disorders (e.g., mood disorders) and neurologic causes (e.g., post-traumatic hypersomnia). An excessive daytime sleepiness with an urge to fall asleep is the hallmark of narcolepsy	Parent/child questionnaires
SDB	A clinical spectrum that includes primary snoring, upper airway resistance syndrome (characterized by snoring and increased respiratory effort), partial obstructive hypoventilation hypopneas (characterized by snoring, increased respiratory effort and arousals), and obstructive sleep apnea (characterized by snoring, apneic pauses and arousals). The diagnosis of SDB requires a polysomnographic recording. Parents may report some of the associated symptoms (e.g., snoring, pauses in breathing, among others)	Parent questionnaires; (home video)
RS	Sleep characterized by excessive movements of some parts of the body or the whole body	Parent questionnaires
PA	Undesirable physical events or experiences that occur during entry into sleep, within sleep or during arousals from sleep. They include sleepwalking, sleep terrors, nightmare disorder, enuresis, sleep-related groaning, among others	Parent questionnaires; home video
Objective parameters		
SOL-PSG	The time in minutes from lights-off to the first epoch of stage 2 sleep	PSG
SOL-a	Time in minutes from getting into bed/lights-out to actigraphically defined sleep onset (the first 10-min interval in which there is activity in no more than one epoch that is above the threshold set for determining 'wake')	Actigraphy
SHIFTS	Number of shifts from one sleep stage to another during the total sleep time	PSG
SHIFTS/h	Number of shifts from one sleep stage to another in a hour of sleep	PSG
ST1%	Disappearance of the EEG α -pattern and the establishment of θ -waveforms (2–7 cps) and slow, eye rolling movement in total sleep time (= total sleep episode less awake time)	PSG
ST2%	The appearance of low frequency, high amplitude discharges (K complexes) and brief high frequency (12–14 cps), variable amplitude discharges (sleep spindles) on a background of θ -waveforms in total sleep time	PSG
SWS%	Percentage of stage 3 sleep (characterized by slow waves, high amplitude, low frequency [0.5–2 cps] δ -waveforms in at least 20% of total sleep time) + stage 4 sleep (characterized by slow waves in more than 50% of total sleep time) in total sleep time	PSG

AHI: Apnea-Hypopnea Index; BR: Bedtime resistance; DMA: Difficulties with morning awakening; DS: Daytime sleepiness; MSLT: Multiple sleep latency test; NA: Night awakening; NW: Night wakings on actigraphy; PA: Parasomnias; PSG: Polysomnography; REM: Rapid eye movement; REM%: Percentage of rapid eye movement; REML: Rapid eye movement sleep latency; RLS: Restless legs syndrome; RS: Restless sleep; SD: Sleep duration; SDB: Sleep-disordered breathing; SE: Sleep efficiency; SE-a: Sleep efficiency assessed with actigraphy; SE-PSG: Sleep efficiency assessed with polysomnography; SHIFTS: Number of stage shifts in total sleep time; SHIFTS/h: Number of stage shifts/hour sleep; SOD: Sleep-onset difficulties; SOL: Sleep-onset latency; SOL-a: Sleep-onset latency evaluated with actigraphy; SOL-PSG: Sleep-onset latency evaluated with polysomnography; ST1%: Percentage of stage 1; ST2%: Percentage of stage 2; SWS%: Percentage of slow-wave sleep; TS: True sleep on actigraphy.

Table 2. Sleep parameters from subjective and objective studies (cont.).

Parameter	Description	Means of assessment
Objective parameters (cont.)		
REML	The time from sleep onset to the first appearance longer than 2 min of REM sleep (defined by rapid bursts of back-and-forth eye motion, muscle atonia and EEG waveform [θ- and β-activity] typical of lighter sleep stages)	PSG
REM%	REM% sleep in total sleep time	PSG
SE-PSG	Ratio of total sleep time to nocturnal time in bed	PSG
SE-a	Ratio of total sleep time to nocturnal time in bed	Actigraphy
TS	Sleep time excluding all periods of wakefulness	Actigraphy
NW	Number of wakings during the night that last at least 5 min	Actigraphy
Average times to fall asleep at MSLT	Means of average times on all MSLT naps and opportunities to fall asleep. The lower it is, the higher the sleepiness during daytime	MSLT
AHI	The number of apnea and hypopnea episodes per hour (apnea is defined as a cessation of airflow for at least 10 s; hypopnea is defined as a 50% reduction in airflow [measured with a validated technique] or a reduction in airflow associated with a 3% fall in arterial oxygen saturation and/or an arousal)	PSG

AHI: Apnea-Hypopnea Index; BR: Bedtime resistance; DMA: Difficulties with morning awakening; DS: Daytime sleepiness; MSLT: Multiple sleep latency test; NA: Night awakening; NW: Night wakings on actigraphy; PA: Parasomnias; PSG: Polysomnography; REM: Rapid eye movement; REM%: Percentage of rapid eye movement; REML: Rapid eye movement sleep latency; RLS: Restless legs syndrome; RS: Restless sleep; SD: Sleep duration; SDB: Sleep-disordered breathing; SE: Sleep efficiency; SE-a: Sleep efficiency assessed with actigraphy; SE-PSG: Sleep efficiency assessed with polysomnography; SHIFTS: Number of stage shifts in total sleep time; SHIFTS/h: Number of stage shifts/hour sleep; SOD: Sleep-onset difficulties; SOL: Sleep-onset latency; SOL-a: Sleep-onset latency evaluated with actigraphy; SOL-PSG: Sleep-onset latency evaluated with polysomnography; ST1%: Percentage of stage 1; ST2%: Percentage of stage 2; SWS%: Percentage of slow-wave sleep; TS: True sleep on actigraphy.

consistent with the report of some patients with ADHD stating ‘Doctor, it is difficult for me to fall asleep at night... if I could choose, I would fall asleep around 2 am!’ and ‘I try to fall asleep at 10:30 pm, but it is simply impossible for me.’

■ Restless legs syndrome & periodic limb movements during sleep

The second objective disorder that can be found in a portion of individuals with ADHD is restless legs syndrome (RLS), a sensorimotor disorder characterized by an irresistible urge to move the legs, often associated with uncomfortable sensations in the legs or, less frequently, other body parts. Although RLS has traditionally been considered as a disorder of middle-to-older age, several studies (summarized in [21]) have shown that it may occur in childhood. **Box 1A–C** summarizes RLS diagnostic criteria in adults and the proposed research criteria for children. In a review of the literature conducted in 2005, Cortese and colleagues found that approximately 44% of subjects with ADHD have been found to have RLS or RLS symptoms, and up to 26% of subjects with RLS have been found to have ADHD or ADHD symptoms [22]. Given the methodological limitations of the included studies (which mostly included participants with RLS and ADHD symptoms, without a formal categorical diagnosis of the two disorders)

these data could not establish if the relationship between ADHD and RLS is one of differential diagnosis or true comorbidity. However, some studies do indicate a true comorbidity between ADHD and RLS in some cases [23,24], although it should be noted that in other cases RLS itself might simply be mimicking ADHD. In cases with true comorbidity, it has been suggested that a common deficiency of iron may underlie both ADHD and RLS symptoms [25]. Of note, iron deficiency has been reported both in RLS and ADHD, although the extent to which there is a peripheral or a central (i.e., in the brain) iron deficiency is still a matter of debate [26,27].

From a clinical standpoint, we note that in our experience [28,29], children with RLS can present with bedtime opposition, probably because they associate bedtime with the occurrence of the unpleasant RLS sensations. Parents and clinicians may consider this as the expression of oppositional defiant disorder, ignoring the true reason underlying the child’s behavior.

In up to 90% of cases, RLS can be accompanied by periodic limb movements in sleep (PLMS), which are repetitive leg jerks characterized by a flexion movement at the ankle, knee and hip that arise from sleep lasting 0.5–10 s, separated by intervals of 5–90 s and occurring subsequently for at least four-times [30]. PLMS may be associated with partial or total arousal

Box 1. Criteria for the diagnosis of restless legs syndrome.

A. International RLS Study Group diagnostic criteria for RLS in adults

- An urge to move the legs usually accompanied or caused by uncomfortable and unpleasant sensations in the legs (sometimes the urge to move is present without the uncomfortable sensations and sometimes the arms or other body parts are involved in addition to the legs)
- The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity, such as lying or sitting
- The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues
- The urge to move or unpleasant sensations are worse in the evening or night than during the day or only occur in the evening or night (when symptoms are very severe, the worsening at night may not be noticeable but must have been previously present)

B. Proposed International RLS Study Group diagnostic criteria for RLS in children

- Criteria for the diagnosis of definite RLS in children:
 - The child meets all four essential adult criteria for RLS and;
 - The child relates a description in his or her own words that is consistent with leg discomfort (the child may use terms such as 'oowies', 'tickle', 'spiders', 'boo-boos' and 'a lot of energy in my legs' to describe symptoms; age-appropriate descriptors are encouraged)

OR

- The child meets all four essential adult criteria for RLS and;
- Two of three following supportive criteria are present (see below). Supportive criteria for the diagnosis of definite RLS in children: sleep disturbance for age; a biological parent or sibling has definite RLS; and the child has a polysomnographically documented periodic limb movement index of five or more per hour of sleep
- Criteria for the diagnosis of probable RLS in children:
 - The child meets all essential adult criteria for RLS, except the criterion stating the urge to move or sensations are worse in the evening or at night than during the day) and;
 - The child has a biological parent or sibling with definite RLS

OR

- The child is observed to have behavior manifestations of lower-extremity discomfort when sitting or lying, accompanied by motor movement of the affected limbs, the discomfort has characteristics of the adult criteria, including: discomfort is worse during rest and inactivity, relieved by movement and worse during the evening and at night) and;
- The child has a biological parent or sibling with definite RLS
- This last probable category is intended for young children or cognitively impaired children who do not have sufficient language to describe the sensory component of RLS
- Criteria for the diagnosis of possible RLS in children:
 - The child has periodic limb movement disorder and;
 - The child has a biological parent or sibling with definite RLS, but the child does not meet definite or probable childhood RLS definition

C. 2011 revised diagnostic criteria for RLS

- The patient presents an urge to move the legs, usually, but not always, accompanied by or felt to be caused by uncomfortable and unpleasant sensations in the legs (in children, the description of these symptoms should be in their own words)
- The urge to move the legs and any accompanying unpleasant sensations begin or worsen during periods of rest or inactivity, are partially or totally relieved by movement, and only occur or are worse in the evening or night than during the day
- The occurrence of the above features is not solely accounted for as symptoms primary to another condition (e.g., myalgia, venous stasis, leg edema, arthritis, leg cramps, positional discomfort and habitual foot tapping)

RLS: Restless legs syndrome.
Data taken from [31, 102].

from sleep, leading to insomnia and/or poor sleep quality via an arousal-mediated disruption of sleep stability in both rapid eye movement and non-rapid eye movement sleep and cycling alternating pattern [31]. While RLS can be diagnosed based on descriptive criteria, the diagnosis of PLMS is based on polysomnographic data. Periodic limb movement disorder (PLMD) is defined as a PLMS index (number of PLMS per hour) ≥ 5 and is associated with an otherwise unexplained sleep–wake complaint [14]. The relationship between ADHD and PLMS is somewhat difficult to define since some studies on PLMS in ADHD utilize the periodic limb movement index (i.e., the number of PLMS per hour of sleep), while others reported data on PLMD. Therefore, in the aforementioned meta-analysis by Cortese *et al.*, it was not possible to pool data on PLMS [18]. However, in a descriptive analysis of the available studies, Cortese *et al.* concluded that children with ‘real’ ADHD may have a pathological frequency of PLMS [18]. Of note, in another meta-analysis of sleep studies of ADHD, Sadeh *et al.* found that children with ADHD have significantly higher prevalence of PLMS than controls [32].

Identifying PLMS/PLMD in individuals with ADHD is of relevance since they can contribute to restlessness during sleep, which was a diagnostic criterion in previous diagnostic definitions of ADHD (DSM-III) [33]. Moreover, since PLMS can fragment sleep, with consequent impact on daytime cognitive and behavioral function, their identification and treatment might ameliorate ADHD symptoms [10]. This hypothesis still requires solid testing.

■ Sleep-disordered breathing

The relationship between SDB and ADHD is, in part, controversial since it is not clear if SDB is associated with ADHD (categorically diagnosed according to DSM criteria) or if it is just a differential diagnosis [34]. The meta-analysis by Cortese *et al.* [18], which included studies utilizing rigorous criteria for ADHD, suggested that values of the apnea–hypopnea index in children with ADHD in the three objective studies retained in the meta-analysis [35–37] were not very elevated (1.00, 5.80 and 3.57, respectively). However, if one assumes, as suggested by Chervin [34], that moderate values of the apnea–hypopnea index between one and five are suggestive of pediatric obstructive sleep apnea deserving clinical attention, our meta-analysis supports a significant

association between ADHD and SDB. Besides the controversy noted for RLS, even if SDB was just a differential diagnosis of ADHD, it is important for the clinician to bear SDB in mind when evaluating patients referred for ADHD.

Assessment of sleep & sleep disturbances in patients referred for ADHD symptoms

Given the association between sleep disturbances and ADHD, we suggest to systematically screen for sleep problems at the first visit, as well as at each visit of follow-up. Based on the aforementioned considerations, we think that it is paramount to systematically inquire for sleep problems not only in patients with an established diagnosis of ADHD, but also in those presenting symptoms of inattention and/or hyperactivity–impulsivity in order to rule out possible sleep disorders, such as RLS or SDB, that may mimic ADHD. A simple screening can be made just with open, nonstructured questions such as: ‘how long does it take to fall asleep?’, ‘do you have unpleasant sensations in your legs while you are in bed?’ and ‘do you feel rested when you wake up in the morning?’ The following difficulties should also be inquired after: bedtime resistance, sleep-onset difficulty, night awakenings, difficulty with morning awakenings, SDB and daytime sleepiness. Besides clinical interviews, several tools are available to help the clinician screen for sleep problems and orient further assessment. As for children, we note the Sleep Disturbance Scale for Children [38] and the Children’s Sleep Habit Questionnaire [39].

The Sleep Disturbance Scale for Children consists of 26 Likert-type items grouped into six categories representing the most common sleep difficulties affecting adolescents and children: disorders of initiating and maintaining sleep, sleep-breathing disorders, disorders of arousal/nightmares, sleep–wake transition disorders, disorders of excessive somnolence and sleep hyperhidrosis (nighttime sweating) [38]. The scale is addressed to children between 6 and 18 years of age. The internal consistency of the scale is high in healthy controls (0.79) and in children with sleep disorders (0.71); the test/retest reliability is adequate for the total ($r = 0.71$) and single-item scores [19].

The Children’s Sleep Habit Questionnaire is a useful sleep-screening instrument to identify both behaviorally and medically based sleep problems in school-aged children [39]. It is a retrospective, 45-item parent questionnaire,

which includes items relating to a number of key sleep domains: bedtime behavior and sleep onset, sleep duration, anxiety around sleep, behavior occurring during sleep and night waking, SDB, parasomnias, and morning waking/daytime sleepiness. Parents are asked to recall sleep behaviors occurring over a 'typical' recent week. Items are rated on a three-point scale: 'usually' if the sleep behavior occurred five- to seven-times per week; 'sometimes' for two- to four-times per week; and 'rarely' for up to once a week. In a study of the psychometric properties of the scale, α -coefficients range from 0.36 (parasomnias) to 0.70 (bedtime resistance) for the community sample, and from 0.56 (parasomnias) to 0.93 (SDB) for the sleep clinic group. Test-retest reliability values were 0.62 and 0.79 [39].

These questionnaires do not include a systematic screening for RLS, in part because this syndrome has been described in children only recently. To this regard, the clinician can refer to the criteria for RLS proposed in the 1995 RLS Diagnosis and Epidemiology Workshop at the NIH [31], as well as the recent Pediatric RLS Severity Scale (children and parent version) [40], which allows the quantification of the severity and impact of RLS symptoms in children. The Pediatric RLS Severity Scale along with other sleep scales can be downloaded at the following website [101]. For adults, we note the Pittsburgh Sleep Quality Index [41], the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome [42] and the Epworth Sleepiness Scale for measuring daytime sleepiness [43]. Besides questionnaires, another subjective tool is the sleep diary, where the patient (or the parents in the case of children) records sleeping and waking times over a period of some weeks (in our experience: 3 weeks). It is relatively feasible to incorporate each of the aforementioned subjective tools in the first, as well as in the follow-up visits. On the other hand, the systematic use of the previously mentioned objective tools (i.e., PSG, actigraphy, multiple sleep latency test and infrared-video analysis) is clearly not possible, owing to logistic and economic reasons. We suggest that the clinician with limited expertise in sleep medicine should contact the sleep specialist to inquire for the possible usefulness of a polysomnographic recording if there is suspicion of SDB (in the case of obesity or chronic cardiovascular or pulmonary disorders [e.g., congenital malformations and asthma] or if patients or his/her relatives report snoring or episodes of

sleep apnea, or a history of adenotonsillectomy in children), sleep-related seizures (i.e., 'complex stereotypic movements during sleep'), sleep-related causes of excessive daytime sleepiness or sleep fragmentation due to frequent nocturnal arousals (including PLMD or report of 'movement of legs' during sleep). A multiple sleep latency test preceded by all-night PSG should be considered to evaluate daytime sleepiness secondary to sleep alterations or as an expression of a primary alteration of arousal, as well as to rule out narcolepsy as a differential diagnosis.

Clearly, patients present not with a diagnosis of a specific sleep disorder, but with a sleep complaint. For example, bedtime resistance, which, in our experience, is the most common sleep complaint associated with ADHD, may be due to limit-setting disorder, RLS or delayed sleep-phase onset. Thus, the appropriate management of sleep complaints in patients with ADHD relies on the correct identification and treatment of sleep disorder(s) or alterations underlying these complaints. To this regard, the goal of the clinician is to perform an accurate diagnosis using subjective and, when necessary, objective tools. For the diagnosis, we suggest referring to the criteria of the International Classification of Sleep Disorders (Second Edition) [11], which also contains criteria specific for children. The therapeutic strategies of sleep complaints should be tailored to the specific underlying disorder. In our experience, it is not infrequent to find ADHD patients with more than one sleep disorder (e.g., limit-setting disorder and sleep-phase delay).

Therapeutic strategies for sleep disorders associated with ADHD

While literature on the association between sleep disturbances and ADHD is increasing, regrettably, evidence to support specific therapeutic choices is still limited. Here, we present the available evidence for the main sleep disorders that underlie sleep complaints in individuals with ADHD. We stress that, before using these specific strategies, appropriate sleep hygiene, independent of the particular disorder, should be implemented [44]. These behavioral strategies include: to avoid naps and caffeinated beverages within 4 h before bedtime, to establish a calming bedtime routine with a regular sleep schedule in a comfortable and darkened environment, to sleep in a room without loud noises and to avoid electronic media use in the evening. **Box 2** reports the main rules of sleep hygiene.

■ Limit-setting disorder & other behavioral disorders

Sciberras *et al.* published the first pilot randomized controlled trial showing the effectiveness of a behavioral program for sleep disturbances in children due to behavioral factors [45]. By analyzing data from 27 families at 5 months post-randomization, most of the parents reported an improvement in bedtime resistance and other challenging behaviors, including delayed-sleep phase, limit-setting disorder, anxiety, sleep onset-association disorder and insomnia, although the improvement in ADHD symptoms was negligible.

The full study is being conducted in 198 children (aged between 5 and 12 years) with ADHD and moderate-to-severe sleep problems [46]. The proposed behavioral sleep intervention consists of two individual, face-to-face consultations and a follow-up phone call with a trained clinician focusing on the assessment and management of child sleep problems. The ADHD Rating Scale, actigraphy and parent report on behavior, daily functioning and school attendance are primary and secondary end points of the study.

Another relevant behavioral program specific for sleep disturbances in ADHD has been proposed by Corkum's group [47]. The three children included in their preliminary case series presented with several sleep disorders, including 'dyssomnias' or 'primary insomnia' defined by DSM-IV criteria as manifesting with behaviors, such as crying, calling out to parents, leaving the bedroom, cosleeping and tantrums [1]. After 5 weeks of treatment, a clinically significant decrease was reported in the severity of the children's dyssomnias, although no changes in ADHD symptoms were noted. These positive results need to be replicated in a blinded randomized study.

■ Delayed sleep-phase disorder

If a delayed sleep-phase disorder underlies sleep-onset difficulties, we suggest using either nonpharmacological options or medications or both. As for pharmacological options, to date, one open-label study [48] and two randomized, double-blind, placebo-controlled studies [49,50] (plus a ~3.5-years follow-up study [51]) have confirmed the efficacy and good tolerability of melatonin in children with ADHD and sleep-onset delay. In our experience, 3 mg of melatonin for children and 5–6 mg for adolescents are effective. There are no data on long-term follow-up.

Box 2. Common sleep hygiene rules.

- Avoid naps within 4 h before bedtime
- Avoid caffeine within 4 h before bedtime
- Have a calming bedtime routine
- Go to bed at approximately the same time every day
- Sleep in a bed that is comfortable
- Sleep in a darkened room
- Sleep in a room where there are no loud noises
- Avoid electronic media use in the evening

Data taken from [44].

In our experience, as well as in that of several colleagues, melatonin can be continued for several years without major problems of tolerability. However, to elucidate this issue, longer follow-up studies are needed. We note that so far zolpidem has not been proven effective for the treatment of sleep-onset delay in ADHD [52]. Ramelteon has been found effective, but can paradoxically fragment sleep and increase daytime sleepiness [53]. Clonidine has been found effective in case series, but randomized, placebo-controlled trials are lacking [54]. We note that clonidine has been associated with bradycardia. Although early reports pointed to possible severe cardiovascular effects [55], a more recent analysis concluded that clonidine, alone or in association with methylphenidate, is safe and well tolerated [56]. With regards to nonpharmacological options, a recent study showed that cognitive-behavioral therapy in combination with bright-light therapy is effective for adolescents with delayed sleep-phase disorder [57], although no such studies have been specifically conducted in individuals with ADHD.

■ RLS & PLMS

Case reports suggest that dopaminergic agents (e.g., levodopa/carbidopa, pergolide and ropinirole) are effective in children diagnosed with both ADHD and RLS/PLMS, and previously treated with psychostimulants with limited efficacy or intolerable side effects [58,59]. However, to date, the limited number of patients treated and the absence of double-blind, placebo-controlled, randomized trials do not allow evidence-based recommendations for treatment to be made, and these agents have not been approved by regulatory agencies in children. A case-series study suggests that levetiracetam may be an effective option for children with ADHD, RLS and interictal epileptic discharges, with reduction of interictal epileptic discharges, ADHD and RLS symptoms [60].

We also note that since iron deficiency has been reported as a contributing etiopathological factor in both RLS [61] and PLMD [62], iron supplementation has been suggested for the management of these disorders. Indeed, preliminary evidence shows the effectiveness of oral iron for PLMS [62] and intravenous iron supplementation for RLS [63]; although a recent meta-analysis concluded that there is insufficient evidence to conclude that iron therapy is beneficial for RLS [64]. However, no randomized controlled trials have been conducted so far in individuals with ADHD and RLS/PLMS, therefore further evidence is needed before recommending iron (*per os* or intravenously) for RLS or PLMD comorbid with ADHD.

Besides pharmacological treatment, common nonpharmacological strategies for the management of RLS are noted: physical exercise, avoidance of sleep deprivation, caffeine and tobacco, and treatment with sedating antihistamines, serotonergic antidepressants and neuroleptics [65].

■ Sleep-disordered breathing

Some studies show a significant improvement not only in breathing parameters, but also in ADHD symptoms in children diagnosed with ADHD plus SDB after adenotonsillectomy [66,67], suggesting that it is worthwhile to screen and treat SDB, which may aggravate ADHD symptoms.

Besides the aforementioned conditions, we remind the clinician to screen and treat comorbid psychiatric disorders that may contribute to sleep disturbances in ADHD. In the case of depressive disorders, citalopram causes fewer negative effects on sleep continuity [58] and may actually improve sleep in depressed patients [68,69]. Nefazodone and mirtazapine may cause significantly less insomnia than selective serotonin

re-uptake inhibitors, although their use may be associated with daytime sleepiness [70].

Furthermore, the clinician is often faced with sleep problems associated with ADHD drugs, in particular stimulants, although there is no definite evidence showing that stimulants are systematically associated with sleep impairment. Some authors have also suggested that they may improve sleep in selected cases [71,72]. However, most of the studies, as detailed in an excellent recent review [73], show dose–response effects on sleep-onset delay for both methylphenidate and amphetamine stimulants. Long-acting α_2 -agonists have been associated with somnolence in 20–40% of cases when used alone, and in 15–20% of cases if associated with psychostimulants, especially at the beginning of the treatment [73]. There is no consensus on how to manage sleep problems associated with stimulants. We present some suggestions based on our experience and indications of a panel of ADHD experts, which are summarized in **Box 3** [74].

Conclusion & future perspective

Sleep problems are associated with ADHD in a sizable proportion of cases. Limit-setting disorder, RLS, SDB, delayed sleep-phase disorder, stimulant medication and comorbid disorders may all contribute to sleep complaints in individuals with ADHD. Therefore, these disorders should be systematically screened for at each visit and treated appropriately.

The two main areas of future research in the field are:

- To better characterize sleep disorders possibly associated with ADHD. For example, very limited research has been conducted on the relationship between ADHD and narcolepsy or parasomnias, despite clinical experience suggesting a possible significant association.

Box 3. Possible strategies to deal with sleep alterations caused by stimulants.

- Simply wait (insomnia due to stimulants attenuates after 1–2 months)
- Adjustment in dose or dosing schedules (e.g., avoid evening stimulant dose)
- Switch to another stimulant formulation or to another stimulant
- Switch to a nonstimulant, such as atomoxetine (initiate at the lowest available dose [10 mg] and titrate slowly to minimize side effects, up to 1.8 mg/kg/day), bupropion (daily maximum dose to obtain sleep improvement: 50–150 mg)
- Add cyproheptadine (2–4 mg orally), trazodone (25–50 mg), mirtazapine (30–45 mg in adolescents) or melatonin (1–6 mg)
- Use clonidine 0.1–0.4 mg/day, in two divided doses (maximum 0.4 mg/day) as a sole drug for ADHD and sleep problems if previous options do not work

Data taken from [74].

Moreover, future research should better address the relationships between ADHD and SDB or RLS/PLMS (i.e., comorbidity or differential diagnosis?);

- The pertinence of the therapeutic strategies for sleep disorders in individuals with ADHD. Randomized controlled trials of pharmacological and nonpharmacological interventions (and of their combination) will be invaluable to inform the clinician, allowing evidence-based decisions in day-to-day clinical practice.

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