

# Comorbidity and confounding factors in attention-deficit/hyperactivity disorder and sleep disorders in children

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**Abstract:** Sleep problems are commonly reported in children with attention-deficit/hyperactivity disorder (ADHD) symptoms. Research data regarding the complex and reciprocal relationship between ADHD and sleep disturbances has now accumulated. This paper is focused on the types of sleep problems that are associated with ADHD symptomatology, and attempts to untangle confounding factors and overlapping symptoms. The goal is also to present an updated overview of the pathophysiology of and treatment strategies for sleep problems in children with ADHD. The review also points out that future research will be needed to clarify further the other psychiatric comorbidities and side effects of medication in order to improve treatment outcomes and prevent misdiagnosis in clinical practice.

**Keywords:** attention-deficit/hyperactivity disorder, sleep, children

## Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most commonly studied and diagnosed psychiatric disorders in children, and is characterized by inattention, overactivity, and impulsivity.<sup>1</sup> ADHD is estimated to affect about 3%–5% of children globally,<sup>2</sup> although prevalence rates may vary depending on whether samples are obtained from community or clinical settings.<sup>3,4</sup> Complaints of sleep problems in children with ADHD are not uncommon. In 1957, Laufer and Denhoff<sup>5</sup> first reported the association between sleep disturbances and ADHD. They noted “Generally, the parents of hyperkinetic children are so desperate over the night problems that the daytime ones pale in significance”. Restless and disturbed sleep were, at one time, part of the Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnostic criteria for ADHD, although the symptoms were eliminated from subsequent DSM editions.<sup>1,6,7</sup> In recent years, there has been growing interest in sleep disorders associated with ADHD. Manifestations of primary sleep disorders may mimic ADHD symptomatology, so might lead to misdiagnosis in clinical practice. Moreover, the primary sleep disorders may exacerbate underlying ADHD symptoms, which might interfere with the treatment and impair daytime performance. In addition, psychotropic medications that are used to treat ADHD may also result in sleep problems, such as sleep initiation difficulty. Therefore, the management of sleep problems in children with ADHD may significantly reduce behavioral symptom severity and improve the quality of life of these children, as well as that of their families.<sup>8</sup>

However, variations in the inclusion criteria and measurements across the studies have impeded our understanding of the ways in which sleep and ADHD interact. This

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review attempts to clarify the potential confounding factors of previous research regarding the relationships between sleep problems and ADHD in children, and outlines some treatment considerations in the management of sleep disturbances in ADHD. We performed a PubMed search from 1994 (when the American Psychiatric Association first published the DSM-IV) to May 2011, using the following key words in various combinations: “ADHD”, “attention-deficit/hyperactivity disorder”, “sleep”, “sleep disorder”, and “children”. References from each relevant paper, including 14 existing reviews of the literature, were examined to determine if any relevant studies had been missed during the database searches. Case reports and descriptive reports without data analysis were excluded in our review.

## Diagnosis and comorbidity in ADHD

Some of the published studies have reported that the prevalence of sleep disturbances and sleep disorders among children with ADHD are significantly higher than in normal controls, but others failed to replicate these findings.<sup>9,10</sup> One possible reason for the inconsistent results may be that the methods used to define ADHD differed across studies, ranging from subjective rating scales for symptoms of hyperactivity/impulsivity and inattention to clinical judgments made by experienced physicians who were following DSM diagnostic criteria. The studies in which ADHD was defined by questionnaires might be confounded by factors such as psychiatric comorbidity.<sup>11</sup> Many studies that applied DSM diagnostic criteria did not exclude or control the effects of psychiatric comorbidity as well. Comorbid disorders frequently associated with ADHD, such as tic disorder,<sup>12</sup> oppositional defiant disorder,<sup>9</sup> depressive disorders,<sup>13</sup> and anxiety disorders,<sup>13–15</sup> may account for some of the sleep disturbances.

## Subjective and objective measures of sleep in ADHD children

Subjective reports of sleep in children with ADHD have primarily been collected through parental-report questionnaires and sleep logs. The data collected usually include: sleep quality and quantity, with variables (Table 1) such as difficulty in sleep initiation and/or sleep onset latency, total sleep time, wake after sleep onset, number of night-time awakenings, and sleep efficiency; sleep habits and bedtime behaviors, like sleep resistance; and symptoms of sleep disorders, including sleep-related breathing disorders and movement disorders. However, the reliability and validity of subjective sleep measurement may be questionable. It has been reported that the sleep data assessed by the Child Behavior Checklist, a

**Table 1** Definition of the sleep parameters

| Sleep parameters                    | Definition  |
|-------------------------------------|---|
| Wake after sleep onset (WASO)       | Amount of total wake time between sleep-onset and final wake-up   |
| Total sleep time (TST)              | Amount of actual sleep time in a sleep period   |
| Sleep onset latency (SOL)           | Time period measured from light-off to the beginning of sleep   |
| Sleep efficiency (SE)               | Ratio of total sleep time to time in bed  |
| Apnea-hypopnea index (AHI)          | An index used to assess severity of sleep apnea based on total number of complete cessations (apnea) and partial obstructions (hypopnea) of breathing occurring per hour of sleep |
| Periodic limb movement index (PLMI) | An index used to assess severity of periodic limb movement disorder based on total number of periodic limb movements occurring per hour of sleep                                  |

measure frequently used to evaluate sleep disturbance among children with ADHD, was incongruent with the data from sleep logs, actigraphy, and polysomnography.

Objective measurements used to study sleep and ADHD include polysomnography and actigraphy. Polysomnography allows researchers to examine basic sleep parameters, sleep architecture (eg, total sleep time, wake after sleep onset, sleep onset latency, sleep efficiency), and pathological indices (eg, apnea-hypopnea index, periodic limb movement index). However, polysomnography requires subjects to sleep within laboratories, which may produce a sleep pattern that differs from their habitual sleep patterns. Prihodova et al<sup>16</sup> pointed out that the “first-night effect” on sleep variables was more significant in the ADHD group than normal controls. Therefore, it might be necessary to record sleep for more than one night to ensure validity of the data. On the other hand, actigraphy assesses sleep patterns through the recording and analyses of activity patterns. It can provide sleep information, such as sleep onset, sleep offset, sleep onset latency, and wake after sleep onset. The biggest advantage of actigraphy is its capacity to collect data from more than 20 consecutive nights in natural settings. Nevertheless, it does not record pathophysiological indices that are necessary for the diagnosis of some sleep disorders. In addition to the disruption of night-time sleep, excessive daytime sleepiness is one of the major clinical characteristics in patients with sleep disorders. Hence, the multiple sleep latency test is also frequently used to measure daytime sleepiness in ADHD.<sup>16–18</sup> The multiple sleep latency test assesses the physiologic sleep tendency by measuring the time it takes to fall asleep when one begins a nap in the absence of alerting factors, such as noise and light.<sup>19</sup>

**Table 2** Published studies utilizing subjective measures of sleep in ADHD

| Study                                     | Sample size (n)  | Age (years) | Study design                                      | Medication  | Measurement  | Major findings   |
|---|--|-------------|---|-------------|--|--|
| <b>ADHD symptoms</b>                      |  |             |   |             |  |  |
| O'Brien et al <sup>31</sup>               | 44 significant ADHD symptoms<br>53 mild ADHD symptoms<br>39 controls   | 5–7         | Cross-sectional, community-based                  | NA          | Parent report  | Subjective sleep disturbances, such as difficulty initiating sleep, restless sleep, night-time awakenings, snoring, and willingness to fall asleep were frequently reported among significant ADHD symptoms in children.   |
| Gau <sup>32</sup>                         | 2463   | 6–15        | Cross-sectional, community-based                  | NA          | Parent and teacher report<br>SHQ, CPRS-R:S, and CTRS-R:S | Dysomnia, SDB, and daytime sleepiness were related to mother's and teacher's reports on child's symptoms of inattention, and hyperactivity/impulsivity. However, parasomnia was only related to mother's reports on ADHD-related symptoms.   |
| Willoughby et al <sup>38</sup>            | 1073   | 2–5         | Cross-sectional, clinic-based                     | NA          | Parent report<br>CBCL                                    | Relationship between hyperactive-impulsive symptomatology and sleep problems was attenuated once ODD/CD, anxiety, and depressive symptom counts were included as additional covariates.  |
| <b>ADHD diagnosis</b>                     |  |             |   |             |  |  |
| Owens et al <sup>33</sup>                 | 46 ADHD<br>46 normal   | 5–10        | Cross-sectional, clinic-based                     | Unmedicated | Parent and self-report<br>CSHQ                           | Sleep disturbances, particularly at bedtime, are frequently reported by both parents and children with ADHD.   |
| Ivanenko et al <sup>34</sup>              | 29 ADHD alone<br>50 ADHD comorbid with mood and anxiety disorders<br>67 mood and anxiety disorders alone<br>28 other psychiatric disorders<br>174 controls | 5–18        | Cross-sectional, clinic-based and community-based | NA          | Parent report<br>CSQ                                     | ADHD group was reported to have longer sleep latency, more night-time awakenings, nightmares, snoring, restless sleep, bedtime resistance, and leg jerks compared with controls. However, sleep complaints were more likely associated with symptoms of mood disturbances and anxiety rather than derived from the presence of ADHD. |
| <b>ADHD comorbid with other diagnosis</b> |  |             |   |             |  |  |
| Corkum et al <sup>35</sup>                | 25 ADHD<br>25 normals  | 7–11        | Cross-sectional, community-based                  | Drug-naïve  | Parent report<br>CSQ-P                                   | ADHD group was reported to have longer sleep duration, more difficulty with sleep onset, awakening in the morning, and bedtime resistance compared with the normal group.  |
| Sung et al <sup>36</sup>                  | 239 ADHD   | 5–18        | Cross-sectional, clinic-based                     | Medicated   | Parent report  | Difficulty falling asleep, resisting going to bed, and tiredness on waking were extremely common in children with ADHD.  |
| Lim et al <sup>37</sup>                   | 114 ADHD<br>60 normals   | 5–13        | Cross-sectional, clinic-based                     | Medicated   | Parent report<br>CBCL                                    | Children with ADHD reported less sleep and more sleep-related problems compared with controls.   |

**Abbreviations:** ADHD, attention deficit/hyperactivity disorder; CD, compulsive disorder; ODD, oppositional defiant disorder; SDB, sleep-disordered breathing; SHQ, Sleep Habits Questionnaire; CTRS-R:S, Conners' Teacher Rating Scale-Revised:Short Form; CPRS-R:S, Conners' Parent Rating Scale-Revised:Short Form; CBCL, Child Behavior Checklist; CSHQ, Children's Sleep Habits Questionnaire; CSQ-P, Child Sleep Questionnaire; Parent Version; NA, not applicable.

Table 3 Studies utilizing objective measures of sleep in ADHD

| Study                           | Sample size (n)  | Age (years) | Study design                                      | Medication       | Measurement                  | Major findings   |
|---------------------------------|--|-------------|---|------------------|------------------------------|--|
| <b>ADHD symptoms</b>            |  |             |   |                  |                              |  |
| Paavonen et al <sup>45</sup>    | 280 children   | 7–8         | Cross-sectional, community-based                  | NA               | Actigraph                    | Children's short sleep duration measured by actigraphs increase the risk for behavioral symptoms of ADHD.  |
| O'Brien et al <sup>31</sup>     | 44 significant ADHD symptoms<br>53 mild ADHD symptoms<br>39 controls | 5–7         | Cross-sectional, Community-based                  | NA               | PSG                          | REM latency and proportion of REM sleep (%TST) were more likely to be affected in the group with significant ADHD symptoms.  |
| <b>ADHD diagnosis</b>           |  |             |   |                  |                              |  |
| Gruber et al <sup>39</sup>      | 38 ADHD boys<br>64 normal boys                                       | 6–14        | Cross-sectional, community-based                  | Medication-naive | Actigraphy and Sleep diaries | No significant differences were found in SOL, WASO, SE, and TST between the ADHD and control groups.   |
| Gruber and Sadeh <sup>40</sup>  | 24 ADHD boys<br>25 normal boys                                       | 7–11        | Cross-sectional, community-based                  | Medication-naive | Actigraphs                   | No significant differences were found between the ADHD and control groups on SOL, WASO, SE, and TST.   |
| Dagan et al <sup>41</sup>       | 12 ADHD<br>12 controls   | 6–12        | Cross-sectional, clinic-based                     | Medicated        | Actigraph                    | SOL and sleep duration were not significantly different between the two groups. However, quiet sleep percentage and SE were found to be significantly lower in ADHD children than in controls. |
| Gruber et al <sup>46</sup>      | 15 ADHD<br>23 controls   | 7–11        | Cross-sectional, community-based                  | Unmedicated      | PSG                          | Children with ADHD had significantly shorter sleep and REM sleep durations, and a smaller percentage of REM sleep of total sleep time compared with controls.                                  |
| Kirov et al <sup>12</sup>       | 22 healthy controls<br>25 ADHD<br>32 TD<br>24 ADHD + TD              | 8–16        | Cross-sectional, clinic-based                     | Unmedicated      | PSG                          | Children with ADHD had significant longer TST, shorter REM sleep, increased REM sleep percentage, and higher number of sleep cycles than children without ADHD.                                |
| O'Brien et al <sup>47</sup>     | 47 ADHD clinic<br>53 ADHD community<br>49 controls                   | 5–9         | Cross-sectional, clinic-based and community-based | Medicated        | PSG                          | ADHD clinic group showed significantly lower spontaneous arousals, longer REM sleep latency, and lower REM sleep percentage than both ADHD community group and controls.                       |
| Picchiatti et al <sup>48</sup>  | 14 ADHD<br>10 controls   | 5–12        | Cross-sectional, clinic-based                     | Unmedicated      | PSG                          | Duration of deep sleep (Stage 3 and 4), and REM sleep was decreased in ADHD compared with control group.   |
| Prihodova et al <sup>16</sup>   | 31 ADHD<br>26 controls   | 6–12        | Cross-sectional, clinic-based                     | Unmedicated      | PSG                          | Basic sleep macrostructure parameters revealed no differences between control and ADHD groups either the first or the second night.  |
| Leclandreux et al <sup>18</sup> | 33 ADHD boys<br>23 learning disorder boys                            | 5–10        | Cross-sectional, clinic-based                     | Unmedicated      | PSG                          | No significant differences in TST, SOL, number of awakenings, and percentage of different stages were found between children with ADHD and controls.   |

|   |  |      |   |                  |                            |  |
|---|--|------|---|------------------|----------------------------|--|
| Konofal et al <sup>49</sup>               | 30 ADHD boys<br>19 learning disorder boys                            | 5–10 | Cross-sectional, clinic-based                     | Unmedicated      | PSG                        | TST, SOL, number of awakenings, and percentage of different stages in PSG did not differ significantly between the two groups.   |
| Cooper et al <sup>50</sup>                | 18 ADHD<br>20 normal controls  | 4–16 | Cross-sectional, clinic-based                     | Unmedicated      | PSG                        | PSG showed normal arousal indexes, and AHI for the ADHD group and normal control group. The sleep architecture was not significantly different between groups.                                       |
| <b>ADHD comorbid with other diagnosis</b> |  |      |   |                  |                            |  |
| Corkum et al <sup>55</sup>                | 25 ADHD<br>25 normal controls  | 7–11 | Cross-sectional, clinic-based                     | Medication-naive | Actigraphy and sleep diary | There were no group differences on TST, WASO, SOL, and night-time awakenings.  |
| Hvolby et al <sup>42</sup>                | 45 ADHD<br>64 psychiatric control group<br>97 health reference group | 5–12 | Cross-sectional, clinic-based                     | Medicated        | Actigraphy                 | There was a significant difference in SOL between the three groups. There were no group differences for TST, WASO, and night-time awakenings.  |
| Wiggs et al <sup>43</sup>                 | 71 ADHD<br>23 healthy controls                                       | 3–15 | Cross-sectional, clinic-based                     | Medication-free  | Actigraphy and sleep diary | The results suggested no significant differences between the groups for wake time, wake episodes, and sleep schedule.  |
| Owens et al <sup>44</sup>                 | 80 ADHD<br>45 healthy controls                                       | 6–14 | Cross-sectional, community-based                  | Unmedicated      | Actigraphy and sleep diary | Compared with the control group, the ADHD group experienced shorter actual sleep time of all epochs scored as sleep, significantly fewer sleep interruptions, but more total interrupted sleep time. |
| Golan et al <sup>17</sup>                 | 34 ADHD<br>32 healthy controls                                       | 7–17 | Cross-sectional, clinic-based                     | Unmedicated      | PSG                        | Sleep architecture did not differ significantly between the groups, with the exception of higher percentage of REM sleep in the ADHD group.  |
| O'Brien et al <sup>47</sup>               | 47 ADHD clinic<br>53 ADHD community<br>49 controls                   | 5–7  | Cross sectional, clinic-based and community-based | Medicated        | PSG                        | There were statistically significant differences between the ADHD community group and the control group in REM sleep latency and percentage of REM.  |
| Miano et al <sup>51</sup>                 | 20 ADHD<br>20 normal controls  | 6–13 | Cross-sectional, clinic-based                     | Medication-naive | PSG                        | Children with ADHD showed significantly reduced sleep duration, increased rate of stage shifts, lower REM sleep percentage, and lower sleep efficiency.  |
| Silvestri et al <sup>52</sup>             | 55 ADHD<br>20 healthy controls                                       | 6–11 | Cross-sectional, clinic-based                     | NA               | PSG                        | Significant difference in percentage of REM, N2%, N3%, SE, TST, and REM latency between ADHD children and controls.  |
| Kirov et al <sup>53</sup>                 | 17 ADHD boys<br>(12 with comorbid disease)<br>17 normal boys         | 8–14 | Cross-sectional, clinic-based                     | Unmedicated      | PSG                        | PSG data showed a significant increase in the duration of the absolute REM sleep and the number of sleep cycles in ADHD group when compared with controls.   |

**Abbreviations:** ADHD, attention deficit/hyperactivity disorder; TD, tic disorder; PSG, polysomnography; REM, rapid eye movement; SOL, sleep onset latency; WASO, wake after sleep onset; SE, sleep efficiency; TST, total sleep time; N2, sleep stage 2; N3, merged the third and fourth stage of sleep; NA, not applicable.

**Table 4** Published studies investigating the relationship between ADHD and RLS in children

| Study                                | Sample size (n)   | Age (years) | Study design                     | Medication  | Measurement                             | Major findings   |
|--------------------------------------|---|-------------|----------------------------------|-------------|---|--|
| <b>ADHD symptoms</b>                 |   |             |                                  |             |   |  |
| Picchietti and Stevens <sup>54</sup> | 18 RLS  | 8–24        | Cross-sectional, clinic-based    | NA          | NIH-specific pediatric criteria         | ADHD (72%) is a common comorbidity of RLS.   |
| Konofal et al <sup>55</sup>          | 12 ADHD + RLS<br>10 ADHD<br>10 controls                                     | 5–8         | Cross-sectional, clinic-based    | Unmedicated | NIH-specific pediatric criteria<br>CPRS | Children with ADHD and a positive family of RLS are at risk of severe ADHD symptoms.   |
| Rajaram et al <sup>57</sup>          | 11 ADHD<br>10 controls  | 5–12        | Cross-sectional, clinic-based    | NA          | Children and parent's reports           | Some ADHD children with growing pains may actually have RLS.   |
| Kotagal and Silber <sup>56</sup>     | 32 RLS  | <18         | Cross-sectional, clinic-based    | NA          | PSG                                     | Inattentiveness was seen in 8 of 32 subjects (25%).  |
| Chervin et al <sup>58</sup>          | 866   | 2–13        | Cross-sectional, community-based | NA          | PSQ<br>CPRS                             | Inattention and hyperactivity in general pediatric patients associated with symptoms of RLS.   |
| Chervin et al <sup>59</sup>          | 27 ADHD<br>43 non-ADHD psychiatry subjects<br>73 general pediatric subjects | 2–18        | Cross-sectional, clinic-based    | NA          | PSQ<br>CPRS                             | Complaint of restless legs and a composite score for daytime sleepiness showed some evidence of an association with inattention and hyperactivity. |
| <b>ADHD diagnosis</b>                |   |             |                                  |             |   |  |
| Picchietti et al <sup>48</sup>       | 14 ADHD<br>10 control   | 5–12        | Cross-sectional, clinic-based    | Unmedicated | PSG                                     | ADHD children's parents (32%) were more likely to have RLS than the control parents.   |

**Abbreviations:** ADHD, attention deficit/hyperactivity disorder; PSQ, Pediatric Sleep Questionnaire; CPRS, Conners' Parent Rating Scale; NA, not applicable; NIH, National Institutes of Health; PSG, polysomnography; RLS, restless legs syndrome.

In the previous review articles on sleep and ADHD,<sup>10,20</sup> it was pointed out that there is a significant discrepancy between subjective and objective reports of sleep in children with ADHD. Owens<sup>21</sup> and Konofal et al<sup>22</sup> suggested that parents of children with behavioral disorders may be more likely to perceive and report higher levels of daytime and sleep-related disruptive behaviors (bedtime struggles, difficulty with morning waking) in a sort of “negative halo effect”. In addition, caregivers are more likely to be sensitive to the side effects of medication, and report sleep-related behavioral problems, such as prolonged sleep-onset latency.

## Impact of ADHD medication on sleep

Stimulant medication is one of the most effective treatments attempted for the management of ADHD.<sup>23</sup> It seems reasonable to assume that the central nervous system (CNS) stimulants prescribed to treat ADHD may adversely affect sleep due to their pharmacological character. For example, both statistically and clinically significant negative impacts have been reported in total sleep time<sup>24</sup> and sleep onset latency<sup>24,25</sup> in children with ADHD under stimulant medication compared with no-medication conditions. However, recent randomized, double-blind, placebo-controlled trials have demonstrated that CNS stimulants do not significantly increase sleep

disturbances in ADHD.<sup>26,27</sup> For example, one study examined sleep-related side effects of medications for children with ADHD and showed that there was a small increase in incidence of prolonged sleep onset latency and shortened total sleep time when a non-CNS stimulant (atomoxetine) was given compared with when a CNS stimulant (methylphenidate) was given.<sup>28</sup> On the contrary, some beneficial effects were also noted in various subjective and objective measures of sleep. In addition, clonidine, a medication that is often prescribed to treat ADHD-related sleep disturbance, was found to alter the duration of a nonrapid eye movement (NREM)-rapid eye movement (REM) cycle.<sup>29</sup>

All in all, CNS stimulants may cause decreased total sleep time and prolonged sleep onset, and also improve sleep quality by consolidating sleep, decreasing nocturnal awakenings, and increasing the percentage of REM sleep.<sup>30</sup> Furthermore, non-CNS stimulants also caused adverse effects on sleep but the effects were relatively mild.

## General sleep disturbances in ADHD

The relationship between sleep disturbances and ADHD has been examined using different measures. In studies based on parents' reports (Table 2), children with ADHD symptoms were found to have more night waking, difficulty initiating sleep,

**Table 5** Published studies investigating the relationship between ADHD and PLMS in children

| Study                                     | Sample size (n)                             | Age (years) | Study design  | Medication  | Measurement   | Major findings  |
|---|---|-------------|---|-------------|---|---|
| <b>ADHD symptoms</b>                      |   |             |   |             |   |   |
| Chervin et al <sup>58</sup>               | 866   | 2–13        | Cross-sectional, community-based                          | NA          | PSQ<br>CPRS   | Inattention and hyperactivity in general pediatric patients were associated with symptoms of PLMS.  |
| Chervin and Archbold <sup>74</sup>        | 113   | 2–18        | Cross-sectional, clinic-based                             | Medicated   | PSG<br>CPRS   | Rate of PLMS showed a linear association with hyperactivity among subjects with SDB, but no association among those subjects without SDB.       |
| <b>ADHD diagnosis</b>                     |   |             |   |             |   |   |
| Picchiatti et al <sup>48</sup>            | 14 ADHD<br>10 controls                      | 5–12        | Cross-sectional, clinic-based                             | Unmedicated | PSG   | Prevalence of PLMS was higher in the children with ADHD than in controls.   |
| <b>ADHD comorbid with other diagnosis</b> |   |             |   |             |   |   |
| Silvestri et al <sup>52</sup>             | 55 ADHD<br>20 healthy controls              | 6–11        | Cross-sectional, clinic-based                             | NA          | Nocturnal video-PSG<br>International RLS Rating Scale | Significant correlations emerged for International RLS Rating Scale scoring, PLMS indices, hyperactivity, opposition scores, and ADHD subtypes. |
| Kirk and Bohn <sup>76</sup>               | 591   | NA          | Cross-sectional, clinic-based                             | NA          | PSG   | Prevalence of PLMS in 28 children with pre-existing diagnosis of ADHD in our population was higher (7.1%) than group prevalence (5.6%).         |
| Huang et al <sup>77</sup>                 | 88 ADHD<br>27 healthy controls              | 6–12        | Cross-sectional, clinic-based                             | NA          | PSG   | Nine (10.2%) of the ADHD group had $\geq 5$ PLMS per hour, but none in the control group.   |
| Golan et al <sup>17</sup>                 | 34 ADHD<br>32 healthy controls              | 7–17        | Cross-sectional, clinic-based                             | Unmedicated | PSG   | Five of the ADHD group had PLMS during sleep (15%) versus none in the control group.  |
| Crabtree et al <sup>75</sup>              | 40 PLMD/ADHD<br>50 PLMD only<br>52 controls | 5–7         | Cross-sectional, Community-based and clinic-based samples | Medicated   | PSG   | Children with PLMD and ADHD had a significantly greater number of arousals associated with PLMS than children with PLMD only.                   |

**Abbreviations:** ADHD, attention deficit/hyperactivity disorder; PSQ, Pediatric Sleep Questionnaire; CPRS, Conners' Parent Rating Scale; PLMD, periodic limb movement disorder; RLS, restless legs syndrome; PLMS, periodic limb movements; SDB, sleep-disordered breathing; PSG, polysomnography.

bedtime resistance, and daytime sleepiness compared with normal control subjects.<sup>31,32</sup> Children with ADHD were also reported to have significantly more bedtime resistance, longer sleep onset latency, shorter sleep duration, more parasomnias, more night waking, and higher level daytime sleepiness by parent's report.<sup>33,34</sup> Children who have ADHD comorbid with other disorders were also reported to have longer sleep duration, more difficulty with sleep onset, more bedtime resistance, more difficulties awakening in the morning, and more nocturnal activities during sleep,<sup>35,36</sup> but another study reported that they sleep less compared with normal subjects.<sup>37</sup> However, one study reported that sleep complaints were more likely associated with symptoms of mood disturbance and anxiety rather than derived from the presence of ADHD.<sup>34</sup> Symptoms of hyperactivity and impulsivity were also reported to have no significant association with parent-reported sleep problems once psychiatric comorbidity was controlled for in another study.<sup>38</sup>

In studies using actigraphy (Table 3), children with ADHD showed no significant difference in sleep onset latency and sleep efficiency compared with controls.<sup>39,40</sup> However, sleep efficiency and the amount of "quiet" sleep was found to be significantly lower in medicated ADHD children than in controls.<sup>41</sup> When looking at ADHD comorbid with other psychiatric diagnoses, results from actigraphy were less consistent. Most of these studies failed to find night-time awakenings that were clearly described in subjective reports.<sup>35,42,43</sup> Only one study indicated that children who have ADHD comorbid with other psychiatric diagnoses experience longer total interrupted sleep time,<sup>44</sup> while another study showed that they experienced significantly longer sleep onset latency.<sup>42</sup> In addition, another study indicated that healthy children with short nocturnal sleep duration as recorded by actigraphy were found to exhibit more symptoms of hyperactivity/impulsivity.<sup>45</sup>

**Table 6** Published studies investigating the relationship between ADHD and SDB in children

| Study                                     | Sample size  | Age  | Study design                                      | Medication | Measurement | Major findings  |
|---|--|------|---|------------|-------------|---|
| <b>ADHD symptoms</b>                      |  |      |   |            |             |   |
| Chervin et al <sup>81</sup>               | 229  | 2–13 | Longitudinal study, clinic-based                  | Medicated  | PSQ<br>CPRS | Snoring and other symptoms of SDB are strong risk factors for future emergence or exacerbation of hyperactive behavior. |
| Gottlieb et al <sup>80</sup>              | 3019   | 5    | Cross-sectional, community-based                  | NA         | CPRS        | Children with SDB symptoms were more likely to have hyperactivity, inattention, and aggressiveness.                     |
| O'Brien et al <sup>31</sup>               | 44 significant ADHD symptoms<br>53 mild ADHD symptoms<br>39 controls | 5–7  | Cross-sectional, community-based                  | NA         | PSG         | SDB was highly prevalent in children with mild ADHD symptoms but not in those with significant ADHD symptoms.           |
| Chervin et al <sup>79</sup>               | 866  | 2–13 | Cross-sectional, community-based                  | NA         | PSQ<br>CPRS | Inattention and hyperactivity were associated with snoring and other symptoms of SDB.                                   |
| Chervin and Archbold <sup>74</sup>        | 113  | 2–18 | Cross-sectional, clinic-based                     | Medicated  | PSG<br>CPRS | Hyperactivity showed no significant associations with the rate of apneas and hypopneas.                                 |
| <b>ADHD comorbid with other diagnosis</b> |  |      |   |            |             |   |
| Huang et al <sup>82</sup>                 | 66 ADHD<br>20 healthy controls                                       | 6–12 | Cross sectional, clinic based                     | Medicated  | PSG         | Inattention and hyperactivity reduced after treating OSA by adenotonsillectomy or treating ADHD with stimulant          |
| Huang et al <sup>77</sup>                 | 88 ADHD<br>27 healthy controls                                       | 6–12 | Cross-sectional, clinic based                     | NA         | PSG         | ADHD had a higher AHI (56.8% AHI > 1, 19.3% AHI > 5) than healthy controls  |
| O'Brien et al <sup>47</sup>               | 47 ADHD clinic<br>53 ADHD community<br>49 controls                   | 5–7  | Cross-sectional, clinic-based and community-based | Medicated  | PSG         | AHI and apnea index did not differ in the 3 groups  |

**Abbreviations:** ADHD, attention deficit/hyperactivity disorder; AHI, apnea-hypopnea index; PSQ, Pediatric Sleep Questionnaire; CPRS, Conners' Parent Rating Scale; OSA, obstructive sleep apnea; PSG, polysomnography; SDB, sleep disordered breathing.

Many studies have tried to compare results of actigraphy with those from subjective reports by parents. Most of them found that subjective reports tended to overestimate sleep disturbances.<sup>42</sup> It is also possible that the sleep disturbances that come to the attention of parents are not best detected by actigraphy.<sup>43</sup> Results highlight the prominence of parent-reported sleep disturbances in children with ADHD and the need for clinicians to screen routinely for the presence of sleep disorders and to assess detailed sleep physiology whenever sleep disturbances are indicated.

With regard to studies using polysomnography (Table 3), one study showed that nonmedicated children with ADHD were significantly different in their total sleep time compared with the control group.<sup>46</sup> Three studies have reported inconsistent findings for REM duration.<sup>12,46,47</sup> One study showed that the duration of stage 3 sleep was shorter in children with ADHD than in controls,<sup>48</sup> while four studies found no significant differences in sleep variables.<sup>16,18,49,50</sup>

Compared with normal controls, children who have ADHD comorbid with other neurological and psychiatric disorders spent decreased time in bed,<sup>51</sup> and had a shorter total sleep time,<sup>51,52</sup> increased REM latency,<sup>47</sup> higher arousal index,<sup>17,52</sup> increased inconsistency in their REM sleep duration,<sup>17,47,51–53</sup> and lower sleep efficiency<sup>52</sup> on polysomnography. Thus, the hypothesis that sleep disturbances and specific changes in sleep macrostructure are connected with pure ADHD does not seem to be supported in this review of the literature.

Even though sleep difficulties might be common in young people with ADHD, results were not consistent across various measures of sleep. There might be many underlying factors which influence the relationship between ADHD and sleep problems. Therefore, correct identification of such factors may facilitate appropriate management of sleep disturbances in this population. The following section reviews the specific primary sleep disorders identified commonly in children with ADHD.



## Sleep disorders in ADHD

### Restless legs syndrome

Restless legs syndrome (RLS) is characterized by uncomfortable leg or body part sensations with an irresistible urge to move the legs. Recent attention focused on the association between ADHD and sleep disorders has led to a series of studies examining RLS in children with ADHD symptoms<sup>54–59</sup> and with confirmed ADHD<sup>48</sup> (Table 4). In a review of the literature,<sup>60</sup> it was concluded that approximately 44% of patients with ADHD have RLS or RLS symptoms, and up to 26% of patients with RLS were found to have ADHD or ADHD symptoms. With the exclusion of “motor restlessness” as part of the diagnostic criteria for RLS in 2003, there is no longer any overlap of the diagnostic criteria for ADHD and RLS,<sup>61</sup> and it has become easier to differentiate these distinct but symptomatically similar conditions.

Several mechanisms have been proposed to explain the association between ADHD (or ADHD symptoms) and RLS.<sup>60</sup> In children, sleep disturbance may precede or overshadow the complaint of leg discomfort.<sup>56</sup> The quality and quantity of a child’s sleep is often diminished with RLS. This sleep deprivation resulting from RLS can cause moodiness, irritability, inattentiveness, fatigue, and hyperactivity.<sup>35,62,63</sup> Therefore, RLS might lead to symptoms of ADHD through sleep disruption. Secondly, diurnal manifestations of RLS, hyperactivity and inattentiveness, might mimic ADHD symptoms or be misclassified as symptoms of hyperactivity.<sup>64</sup> A third possibility is that RLS and ADHD might share a common pathology, such as a dopaminergic deficit.<sup>58</sup> Such a possibility is supported by the previous open-label studies, showing that children with symptoms of RLS and ADHD could benefit from treatment with dopaminergic agents.<sup>65,66</sup> However, the first double-blind study of a dopaminergic therapy found that L-dopa significantly improved symptoms of RLS and periodic limb movement disorder (PLMD) symptoms but not ADHD.<sup>67</sup> Because there were methodological limitations, including small sample size and inability to control for baseline differences in severity of ADHD symptoms, these results should be interpreted carefully and future studies are needed to address this issue further. The fourth explanation is that both ADHD and RLS are associated with iron deficiency.<sup>56,68,69</sup> The findings described here are consistent with pathophysiological models of these disorders because iron is needed for dopamine synthesis.<sup>70</sup> While dopaminergic agents are not approved for use in children with RLS, another possible implication of the association between RLS and ADHD symptoms concerns iron supplement treatment. Incidentally, iron supplementation has been reported

to improve symptoms in children with ADHD with an iron-deficient diet.<sup>71</sup> Moreover, Konofal et al<sup>72</sup> have pointed out that iron supplementation appeared to improve ADHD symptoms in children with low serum ferritin levels.

### Periodic limb movements

Periodic limb movements (PLMS) is objectively defined as the presence of repetitive movements of the toes, feet, legs, thighs and arms that last 0.5–5.0 seconds and occur at 5–90 second intervals during sleep. According to the reports, 80% of patients with RLS also have characteristic leg movements during sleep that meet the diagnostic criteria for PLMS.<sup>73</sup> Several investigators have reported excessive PLMS in association with ADHD symptoms<sup>58,74</sup> (Table 5). The prevalence of PLMS in children diagnosed with ADHD is estimated to be as high as 7%–44%, compared with a prevalence of only 1.2%–2.0% in pediatric populations at risk for sleep disorders.<sup>48,52,75,76</sup> Moreover, Huang et al<sup>77</sup> and Golan et al<sup>17</sup> found on polysomnography that 10.2%–14.7% of children with ADHD comorbid with other diagnosis had PLMD compared with 0% of controls. Children with PLMD during sleep can have sleep fragmentation that can lead to increased risk of inattention and hyperactivity, which are two major symptoms of ADHD. Chervin et al<sup>58</sup> further reported a dose-dependent relationship between PLMS scores on the Pediatric Sleep Questionnaire and hyperactivity index on the Conners’ Parent Rating Scale-Short Form. Crabtree et al<sup>75</sup> also showed that children with PLMD and ADHD were more likely to have PLMS-related arousals than children with PLMD only. Thus, Crabtree et al<sup>75</sup> postulated that the link between ADHD and PLMD may be mediated by sleep fragmentation associated with PLMS-induced arousals and the presence of reduced REM sleep.

In addition, ADHD, RLS, and PLMS are all associated with low iron stores.<sup>68,78</sup> The finding of relative iron deficiency is consistent with pathophysiological models of these disorders because iron is needed for dopamine synthesis. Walters et al<sup>65</sup> indicated the treatment of PLMD with dopaminergic agents in the absence of psychostimulant use resulted in marked improvements in PLMD and ADHD. Thus, both PLMS and ADHD have been shown to be related to dopamine production and metabolism.

### Sleep-disordered breathing

Sleep-disordered breathing (SDB) in children includes a spectrum of disorders that vary in severity, ranging from obstructive sleep apnea at one end to primary snoring, ie,

snoring without ventilator abnormalities. Several studies have demonstrated the association between symptoms of SDB and ADHD-related symptoms,<sup>31,47,77,79–81</sup> but others have failed to show the association<sup>74,82</sup> (Table 6). The inconsistent results were probably due to the difference in criteria used to diagnosis SDB (apnea-hypopnea index <1 or <5), as well as the aggravating effect of SDB on ADHD. Repeated episodes of nocturnal hypoxia in SDB comprise an important causal factor for neurobehavioral deficits. Sleep fragmentation resulting from frequent nocturnal arousals may also lead to daytime symptoms.<sup>21</sup> Both neurobehavioral deficits and daytime symptoms might mimic or exacerbate the cardinal symptoms of ADHD.

Regarding treatment strategies in this population, both Huang et al<sup>82</sup> and Dillon et al<sup>83</sup> reported that behavioral morbidity in children with ADHD and SDB improved significantly more after adenotonsillectomy than after stimulant treatment. These results suggest that appropriate recognition and surgical treatment of underlying SDB in children with ADHD might prevent the need for long-term stimulant treatment.<sup>82</sup> A recent longitudinal study has shown that improvements were maintained 2.5 years after surgery.<sup>84</sup>

## Conclusion

ADHD-related symptoms are frequently associated with sleep problems/disorders. In our literature review, sleep disturbances are less supported by objective sleep measurements in pure unmedicated ADHD. Therefore, evaluation of other psychiatric comorbidities and the side effects of medications is necessary when assessing the causes of their sleep complaints. Moreover, sleep disturbance is very complex, especially in ADHD children. It is critical for health providers caring for this population to identify correctly the exact abnormality in sleep disturbance within this group of children. Success in treating sleep disturbance in this population depends on accurate diagnosis of the exact sleep disturbance and its pathology. Our review shows that successful management of sleep problems/disorders results in considerable improvement in the level of daytime impairment. Future studies addressing the causal relationship between sleep problems and ADHD-related symptoms should take into account potential confounding variables and include better controls. In addition, research focused on surgical management (adenotonsillectomy) and iron supplementation should not only focus on reduction of the apnea-hypopnea index and the periodic limb movement index as the primary parameters of a successful treatment outcome, but also consider other measures of sleep disturbance.

## Disclosure

The authors report no conflicts of interest in this work.

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