



CLINICAL REVIEW

Sleep in children with attention-deficit hyperactivity disorder: A meta-analysis of polysomnographic studies

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KEYWORDS

Sleep;
ADHD;
Attention deficit;
Hyperactivity;
Children;
Review

Summary The links between sleep and attention-deficit hyperactivity disorder (ADHD) have been a topic for intense ongoing research and clinical interest. Previous narrative literature reviews conveyed a consensus that parents of children with ADHD are more likely to report sleep problems in their children in comparison to parents of control children. However, when objective measures are considered the results appear to be more complex and inconsistent. This review is based on a meta-analysis of relevant polysomnographic studies. We assessed measures related to sleep architecture, breathing disorders, and periodic limb movements in sleep (PLMS), and the role of potential moderators such as age, gender, and other methodological factors. The meta-analysis revealed only one significant combined effect that indicates that children with ADHD are more likely than controls to suffer from PLMS. Factors such as age, gender, inclusion of adaptation night, and comorbidity appear to play a moderating role in the associations between sleep characteristics and ADHD. To provide new insight regarding the links between sleep and ADHD research in this field should adopt new strict guidelines and consider the role of multiple pertinent moderating factors.

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Introduction

The associations between sleep and attention-deficit hyperactivity disorders (ADHD) have been a focus for clinical and empirical efforts over the last

two decades. A number of narrative literature reviews addressed this issue in recent years.^{1–5}

These reviews conveyed the conclusion that the basic question of whether children diagnosed with ADHD have unique sleep characteristics is far from being resolved. For instance, a recent study concluded that sleep of children with ADHD is not distinct from normal sleep,⁶ leading to a strong

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Nomenclature		PLMD	Period limb movement disorder
ADD	Attention deficit disorder	PLMS	Periodic limb movements in sleep
ADHD	Attention-deficit hyperactivity disorder	PSG	Polysomnography
AHI	Apnea–hypopnea index	RDI	Respiratory disturbance index
AI	Apnea index	REM	Rapid eye movement sleep
DSM	Diagnostic and statistical manual of mental disorders	RLS	Restless leg syndrome
ICD	International Statistical Classification of Diseases and Related Health Problems	SWS	Slow wave sleep
		TST	Total sleep time

rebuttal.⁷ To shed more light on this issue we performed a meta-analysis on the available polysomnographic studies of children with ADHD.

Difficulties in defining and diagnosing ADHD

The definition and diagnostic criteria of ADHD has evolved over the last few decades. Currently, the diagnosis of ADHD relates to three major domains of difficulty: attention problems, impulsivity, and hyperactivity. Subtypes of ADHD diagnosis have been identified according to the dominant areas of difficulty: a predominantly hyperactive–impulsive type, a predominantly inattentive type, and a combined type.⁸ The specific symptoms associated with each domain and type are listed in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV),⁸ and in the International Statistical Classification of Diseases and Related Health Problems (ICD-10).⁹

In the context of the associations between ADHD and sleep, it is important to note that in earlier editions of the DSM, sleep problems were considered as a diagnostic symptom of ADHD. However, this association was excluded from the latest editions (DSM III revised and DSM IV).

ADHD as a clinical entity has been a topic for scientific and public controversy (e.g., Refs. ^{10–12}). The definition of ADHD and the diagnostic procedures and criteria employed involve complex conceptual and methodological issues.^{13–15} Although symptom checklists have been defined and the use of multiple sources of information have been recommended there are no clear guidelines as to how to integrate these sources of information.¹⁴ This state of affairs leads to a large variability in diagnostic methods and directly affects even the most basic questions such as the prevalence of ADHD. Based on different diagnostic classifications and methodologies the prevalence of ADHD has been estimated to range between 5% and 20%.^{13–16} More

recent prevalence rates range between 8%–12%.¹⁴ Variability in diagnostic procedures has direct impact on any ADHD-related research including the research on the links between sleep and ADHD.

The clinical picture of ADHD changes with age. With maturation, some of the manifestations of ADHD (particularly hyperactivity) decrease or even disappear in some children.^{14,17} In the earlier stages of ADHD research, this observation led to a belief that ADHD is a developmental disorder that disappears with brain maturation. However, longitudinal research has shown that more than 50% of the children with ADHD grow-up to be adults with significant ADHD-related symptoms.^{14,17} Taking into account maturational changes in the manifestation of ADHD is particularly important in the context of research on potential links between ADHD and other neurobehavioral systems that undergo significant maturational changes during childhood (e.g., the sleep–wake system).

Another important factor in ADHD is gender. ADHD is more prevalent in boys than in girls, who represents 1 in 10 in clinical samples and 1 in 3 in community samples.^{13,18} Gender also appears to influence the clinical manifestations of ADHD.^{13,18} For instance, girls with ADHD are less likely than boys to have a comorbid disruptive behavior disorder. Such gender-specific clinical manifestations of ADHD may have significant implications for research, as different gender representations in research samples may influence the results if gender is not controlled for or its effects are not specifically assessed.

Finally, the diagnosis of ADHD is closely associated with other clinical disorders. Common comorbidity includes oppositional defiant disorder, conduct disorder, mood disorders, anxiety disorders and learning disorder.^{16–18} The comorbidity rates in childhood are high ranging between 20% and 30% of children with ADHD for learning, anxiety, mood, and conduct disorder, and reaching more than 50% comorbidity rate with oppositional defiant disorder in boys.¹³ Therefore, the problem of disentangling

the distinct features of ADHD from the features of the associated disorders is probably one of the most complicated methodological problems in ADHD research.

ADHD and sleep

Studies assessing the links between sleep and ADHD could be broadly characterized by a number of factors: (a) sleep assessment method (e.g., self or parental reports, polysomnography, actigraphy); (b) specific sleep-related domain (e.g., sleep architecture; sleep disordered breathing, PLMS or PLMD); (c) comparison method (e.g., comparing sleep in children with and without a diagnosis of ADHD; comparing ADHD symptoms or diagnosis in children with and without sleep problems; or correlative studies associating sleep- and ADHD-related measures).

Previous narrative literature reviews have drawn a clear distinction between studies based on objective (PSG, actigraphy) and subjective (parental reports) measures.¹⁻³ There appears to be a consensus among reviewers that parents of children diagnosed with ADHD are more likely to report sleep-related problems in their child than parents of control children.¹⁻⁵ However, when objective sleep measures are considered the analysis is more challenging and the conclusions are more tentative. For instance, Cohen-Zion and Ancoli-Israel concluded that: "...actigraphic and PSG data have not identified clear and consistent differences in measures of sleep continuity or sleep architecture between children with or without ADHD."² Van der Heijden et al.⁴ summarized their conclusions in a different way: "There is high evidence that disturbances in sleep architecture can be found in ADHD; however there is no specific disturbance related to ADHD."

To facilitate the understanding of the complex and somewhat conflicting and inconsistent results derived from PSG studies, we focus our meta-analytic review on PSG studies comparing sleep in children diagnosed with ADHD. Our analysis includes three controversial areas: (a) sleep architecture; (b) sleep disordered breathing; and (c) PLMS or PLMD.

Our review of the literature as well as previous literature reviews on PSG studies in children with ADHD have highlighted a number of conceptual and methodological factors that could seriously confound the research in this area. These factors include: (a) the definition and diagnosis of ADHD which appear to significantly diverge across studies; (b) the wide age ranges of participants

included in these studies; (c) gender representation in the samples; (d) source of patient referrals (i.e., psychiatric clinic, community sample, or sleep lab referral); and (e) number of PSG nights (with or without adaptation night). Our meta-analysis was designed to assess if the inclusion of these factors, and their evaluation as moderating variables could facilitate the understanding of the non-consistent results summarized in previous reviews.

Methods

Literature base

Studies were collected through a computerized search of the PsycInfo, PubMed and ISI Web of Science databases using the key words "ADHD" or "Attention deficit and hyperactivity disorder", "hyperactivity" or "attention deficit" intersected with PSG, or polysomnography, or EEG and intersected with Sleep. Additionally, these databases were searched with the names of researchers in the field to see whether there were additional relevant papers from these authors. The references of all obtained articles were systematically searched for additional relevant studies, as well as the references of relevant review papers (e.g., Refs. ¹⁻⁵).

Criteria for selecting studies

We used the following criteria to select studies for the meta-analysis:

1. The study was published as a journal article in the English language from January 1980 until October 2005. The selection of 1980 as the low cutoff for inclusion in the meta-analysis corresponds to the publication year of DSM-III. We found the definitions and diagnostic criteria for ADHD in the few relevant studies published prior to this year to be rather ambiguous relative to current diagnostic criteria. In addition, these studies tended to use very small sample sizes (e.g., $n = 3$),¹⁹ and usually did not report sufficient data to allow computation of effect sizes.^{20,21}
2. The study contrasted sleep parameters of a group of children diagnosed with ADHD or ADD with those of a group of control children. Studies without an integral control group were not included in the meta-analysis (e.g., Refs. ^{6,22}). Also excluded was one study that compared the recordings of an ADHD group with data from a normative sample reported elsewhere.²³

3. The independent variable (ADHD or lack-there-off) was not confounded with the dependent variables (sleep indices). That is, sub-samples of children with ADHD who were recruited out of samples of children who were first suspected as having a sleeping disorder were excluded from the meta-analysis. For example, in a study by Picchietti et al.,²⁴ children recruited into the ADHD group were those suspected for having PLMD.
4. The study used polysomnographic recording to assess at least one of the following PSG measures: sleep efficiency, sleep latency, total sleep time (TST), percentages of Stage 1, Stage 2, slow wave sleep (SWS), and rapid eye movement sleep (REM), REM latency, number of arousals, periodic limb movements (PLMS), apnea index (AI/OSA), and apnea-hypopnea index (AHI/RDI).
5. The study provided data that allowed the computation of a between-groups effect size for at least one of the above PSG measures by reporting means and standard deviations of the two groups, or statistics such as t , F , or χ^2 values.

Application of these criteria resulted in a selection of 12 samples reported in 11 journal articles, including 333 children with ADHD and 231 control children. The studies included in the meta-analysis and their effect sizes are listed in Table 1.

Coding system and coding decisions

A standard coding system was used to rate every candidate study (Table 2). We coded sample size (n) of the ADHD and the control groups, and whether the groups included males and females or only males (*Gender*). We also coded whether the *average age* of the sample was younger than 9 years or older. In addition, we noted whether *subjects' recruitment* took place in a general clinic or in a sleep clinic, and whether means were taken to ensure the absence of children with ADHD in the control group (*Control Group Screening*). We were interested in whether DSM criteria were applied in the *diagnosis* of ADHD or whether no such standard criteria were used. In order to assess the effect of comorbid disorders on the sleep patterns of children with ADHD we coded whether participants with comorbid disorders were included or excluded from each sample (*Comorbidity*). In this meta-analysis, the coding of comorbidity refers to the exclusion of psychosis, affective, or anxiety disorders. Patients with disorders that share high

comorbidity rates with ADHD such as learning disabilities, conduct disorder, and oppositional defiant disorder were either included or the studies did not mention these disorders as an exclusion criterion. Finally, we coded the rates of *medication* use in the ADHD group, and noted whether the sample consisted of non-medicated participants (0% medicated) or whether at least some of the participants of a sample were treated with medications (four of the seven medicated sample reported that 100% of the participants were medicated).

Some additional coding decisions were made:

1. Most studies presented sleep stages data as the percentage of each stage from the total sleep time. If a difference between groups based on percentages was reported, or alternatively, could have been computed, we used this measure. Some studies (e.g.,^{25,26}) reported between group contrasts relying on absolute time for each stage, without percentage data. We used these data to calculate effect sizes provided that no between groups difference in total sleep time could be verified.
2. When appropriate, we combined effect sizes of separate measures to allow comparable results across studies. For example, when sleep stages 3 and 4 were reported separately we combined the effect sizes to reflect the outcome of slow wave sleep.²⁶ In another example we combined effect sizes from data reported separately for several nights.²⁶
3. When one control group was compared with two ADHD groups within the same study, the number of control participants was split accordingly in order to avoid overlap of subjects.²⁷
4. If there was an overlap between participants in studies reported in more than one article, only the data from one article was used in the meta-analysis (e.g., Konofal et al.²⁸ and Lecendreux et al.²⁹).

Meta-analytic procedures

The effect size index we used in the present meta-analysis is *Cohen's d*, the difference between the means of two groups, divided by their pooled standard deviation. A positive sign of d was assigned for all PSG measures if the ADHD group scored higher than the control group. A negative sign of d was assigned if the opposite was true. All analyses and computations were carried out using the Comprehensive Meta-Analysis (CMA) software, Version 2.002 (Biostat, Englewood, NJ, USA).

Table 1 Studies used in the meta-analyses

Study	<i>n</i> ADHD	<i>n</i> Control	Male %	Average Age	Age Range	Recruitment	ADHD diagnosis	Medication %	PSG measure	<i>d</i>
Busby et al. ²⁶	11	11	100	10.6	8–12	—	DSM III	0	TST	0.211
									Sleep efficiency	-0.163
									Sleep latency	0.249
									Stage 1	0.029
									Stage 2	0.418
									SWS	-0.298
									REM	-0.283
									REM latency	1.049
									AI	—
									AHI/RDI	—
Cooper et al. ⁵⁵	18	20	68.4	10.24	4–16	—	DSM IV	Medicated, % not reported	TST	—
									Sleep efficiency	0.025
									Sleep latency	—
									Stage 1	0.129
									Stage 2	-0.275
									SWS	0.027
									REM	0.435
									REM latency	0.279
									AI	0.221
									AHI/RDI	0.225
Golan et al. ⁵⁶	34	32	71.2	12.2	—	Clinic referral	DSM IV	100	TST	0.261
									Sleep efficiency	0.195
									Sleep latency	-0.249
									Stage 1	—
									Stage 2	—
									SWS	0.074
									REM	0.547
									REM latency	—
									AI	—
									AHI/RDI	0.670
Greenhill et al. ²⁵	9	11	65	8.98	6.7–11.8	Clinic referral	DSM III	100	TST	-0.009
									Sleep efficiency	-0.494
									Sleep latency	0.269
									Stage 1	—
									Stage 2	—
									SWS	—
									REM	—
									REM latency	—
									AI	—
									AHI/RDI	—

Table 1 (continued)

Study	n ADHD	n Control	Male %	Average Age	Age Range	Recruitment	ADHD diagnosis	Medication %	PSG measure	d
Huang et al. ⁵⁷	88	27	85.2	8.59	—	Clinic referral	DSM IV	Medicated, % not reported	Stage 1	-0.189
									Stage 2	-0.103
									SWS	0.126
									REM	-0.278
									REM latency	-0.045
									AI	—
									AHI/RDI	—
									PLMS	—
									Arousals	—
									TST	-0.463
Khan ⁵⁸	16	12	100	8.37	6-12	Clinic referral	No standard criteria	100	Sleep efficiency	-0.393
									Sleep latency	0.391
									Stage 1	0.388
									Stage 2	-0.371
									SWS	-0.215
									REM	-0.126
									REM latency	-0.09
									AI	—
									AHI/RDI	0.546
									PLMS	0.303
Arousals	—									
TST	0.606									
Kirov et al. ⁵⁹	17	17	100	11.2	8-14.4	Clinic referral	DSM IV	82.3	Sleep efficiency	0.439
									Sleep latency	0.535
									Stage 1	0.157
									Stage 2	-0.081
									SWS	0.691
									REM	-1.585
									REM latency	—
									AI	—
									AHI/RDI	—
									PLMS	—
Arousals	—									
TST	0.652									
Sleep efficiency	0.000									
Sleep latency	-0.149									
Stage 1	-0.686									
Stage 2	-0.242									
SWS	-0.050									

Lecedreux et al. ²⁹	30	22	100	8.05	5-10	Clinic referral	DSM IV	0	REM latency	0.528
									AI	-0.405
									AHI/RDI	—
									PLMS	0.252
									Arousals	0.703
									TST	0.042
									Sleep efficiency	-0.025
									Sleep latency	0.138
									Stage 1	0.385
									Stage 2	0.084
								SWS	-0.188	
								REM	-0.250	
								REM latency	0.166	
								AI	—	
								AHI/RDI	—	
								PLMS	—	
								Arousals	-0.043	
								TST	-0.346	
O'brien et al. ^{31*}	53	27	59.4	6.75	3.5-8.3	Ss from both clinic and community	No standard criteria	100	Sleep efficiency	-0.056
									Sleep latency	0.073
									Stage 1	—
									Stage 2	—
									SWS	0.000
									REM	-0.584
									REM latency	0.330
									AI	—
									AHI/RDI	-0.423
									PLMS	0.132
								Arousals	-0.158	
								TST	-0.250	
O'brien et al. ^{31*}	34	26	47.1	6.6	4.6-11.6	Ss from both clinic and community	No standard criteria	0	Sleep efficiency	-0.112
									Sleep latency	0.143
									Stage 1	—
									Stage 2	—
									SWS	0.195
									REM	-0.482
									REM latency	0.190
									AI	—
									AHI/RDI	-0.518
									PLMS	0.151

Table 2 Coding system for individual studies

Variable	Coding description
N ADHD	Sample size of ADHD group
N Control	Sample size of control group
Gender	0 = The sample include males and females 1 = The sample include only males
Average age	0 = Average age of the sample is younger than 9 years 1 = Average age of the sample is older than 9 years
Subjects recruitment	0 = ADHD group was recruited from referrals to a general clinic 1 = ADHD group was recruited from referrals to a sleep clinic
Control group screening	0 = Control participants were screened for ADHD 1 = Screening procedure for the control group is not reported
Diagnosis	0 = No standard criteria were applied in the diagnosis of ADHD 1 = DSM (III or IV) criteria were applied in the diagnosis of ADHD
Comorbidity	0 = Participants with comorbid disorders were excluded 1 = Participants with comorbid mood disorder were included or the comorbidity in the sample was not reported.
Medication	0 = ADHD sample included medicated participants 1 = ADHD sample included non-medicated participants

We present the combined effect sizes and their confidence intervals in the context of either random or fixed model. When a test of data heterogeneity (estimated using the Q statistic) showed that samples included in a comparison were not significantly heterogeneous we used the fixed model. In contrast, when at least one of the levels of a moderator consisted of a heterogeneous set of samples we presented random effects, which are somewhat more conservative than fixed effects parameters in such cases. We computed effect sizes for each PSG measure separately and preformed separate meta-analyses for each measure.

Results

Table 3 provides a detailed description of the results of the overall effect sizes as well as all tests of moderators for each PSG measure. A minimum of 3 studies per condition was set for moderator analyses. For each analysis, number of studies (k), number of participants in each group (n), effect size (d), 95% confidence interval, and p value are reported. In the text below, we address only the significant findings. We describe first the only significant global effect with regard to PLMS, and then address the significant role of different moderators.

Periodic limb movement in sleep (PLMS)

The only PSG measure to show a small but significant overall effect size was PLMS, $d = 0.26$, $p < 0.05$, $CI = 0.04, 0.49$. Children with ADHD displayed more

PLMS during sleep than control children. However, this finding should be taken with great caution because a calculation of fail-safe number revealed that only 7 additional polysomnographic studies with only null results may be sufficient to reduce this effect to insignificance. This number is more than 6 fold lower in comparison with Rosenthal's fail-safe number, $5k + 10 = 45$ ($k = 7$, number of studies included in the PLMS calculation).³⁰

Age

In younger samples (average age < 9 years) children with ADHD had shorter total sleep time than controls ($d = -0.19$, $CI = -0.42, 0.03$); whereas in older samples (average age > 9 years) children with ADHD had longer total sleep time ($d = 0.26$, $CI = -0.02, 0.53$). While each of these combined effect sizes was not statistically significant, the difference between the combined effects was, $Q = 6.15$, $p < 0.05$.

In addition, in younger samples, children with ADHD had significantly longer stage 1 sleep than controls ($d = 0.35$, $p < 0.05$, $CI = 0.05, 0.64$); whereas in older samples children with ADHD tended to have shorter stage 1 sleep ($d = -0.21$, $CI = -.51, 0.09$). The combined effects sizes related to stage 1 sleep where significantly different between the two age groups, $Q = 6.82$, $p < 0.05$.

Although these findings may suggest that the association between ADHD and total sleep time and stage 1 sleep is modulated by age, great caution in interpretation is advised yet again. First, although the combined effect sizes of younger and older children

Table 3 Meta-Analytic Results

	<i>k</i>	<i>n</i> ADHD	<i>n</i> Control	<i>d</i>	95% CI	<i>Q</i> [†]
Total sleep time						
<i>Total data set</i>	10	301	201	-0.01	-0.19, 0.16	
Gender						
Male and female sample	6	227	139	-0.17	-0.39, 0.04	6.57*
Male only	4	74	62	0.30*	0.006, 0.60	
Average age						
Younger than 9 years	6	230	125	-0.19	-0.42, 0.03	6.15*
Older than 9 years	4	71	76	0.26	-0.02, 0.53	
Subjects recruitment						
General referrals	4	144	77	-0.08	-0.37, 0.21	0.03
Sleep clinic referrals	3	121	85	-0.11	-0.39, 0.17	
Diagnosis						
No standard criteria	4	112	81	-0.11	-0.39, 0.17	0.83
DSM	6	189	120	0.05	-0.17, 0.27	
Comorbidity						
Excluded	6	163	99	-0.02	-0.25, 0.21	0.006
Included/Not reported	4	138	102	-0.004	-0.26, 0.26	
Medication						
Medicated	6	217	126	0.04	-0.28, 0.36	0.01
Non-medicated	4	84	75	0.006	-0.37, 0.38	
Adaptation night						
No	6	227	139	-0.18	-0.39, 0.04	6.57**
Yes	4	74	62	0.30*	0.006, 0.60	
Sleep efficiency						
<i>Total data set</i>	11	317	219	-0.09	-0.25, 0.08	
Gender						
Male & female sample	8	259	169	-0.10	-0.89, 0.10	0.008
Male only	3	58	50	-0.08	-0.40, 0.24	
Average age						
Younger than 9 years	5	214	113	-0.19	-0.42, 0.04	1.38
Older than 9 years	6	103	106	0.01	-0.23, 0.25	
Recruitment source						
General clinic	5	158	87	-0.24	-0.51, 0.04	1.55
Sleep clinic	3	121	85	0.01	-0.27, 0.29	
Diagnosis						
No standard criteria	3	96	69	-0.12	-0.32, 0.08	0.29
DSM	8	221	150	-0.02	-0.32, 0.27	
Comorbidity						
Excluded	5	147	87	-0.18	-0.43, 0.06	0.99
Included/Not reported	6	170	132	-0.01	-0.24, 0.22	
Medication						
Medicated	6	219	134	-0.10	-0.33, 0.12	0.02
Non-medicated	5	98	85	-0.08	-0.33, 0.18	
Adaptation night						
No	8	259	169	-0.010	-0.29, 0.10	0.008
Yes	3	58	59	-0.08	-0.40, 0.24	
Sleep latency						
<i>Total data set</i>	10	301	201	0.17	-0.01, 0.35	
Gender						
Male & female sample	6	227	139	0.18	-0.03, 0.40	0.04
Male only	4	74	62	0.14	-0.20, 0.48	
Average age						
Younger than 9 years	6	230	125	0.25*	0.02, 0.47	1.30
Older than 9 years	4	71	76	0.03	-0.28, 0.33	
Subjects recruitment						

Table 3 (continued)

	<i>k</i>	<i>n</i> ADHD	<i>n</i> Control	<i>d</i>	95% CI	<i>Q</i> [†]
General referrals	4	144	77	0.25	−0.04, 0.54	1.61
Sleep clinic referrals	3	121	85	−0.01	−0.29, 0.27	
Diagnosis						
No standard criteria	4	112	81	0.23	−0.05, 0.51	0.30
DSM	6	189	120	0.13	−0.11, 0.37	
Comorbidity						
Excluded	6	163	99	0.37*	0.11, 0.62	4.96*
Included/Not reported	4	138	102	−0.03	−0.29, 0.23	
Medication						
Medicated	6	217	126	0.13	−0.10, 0.36	0.30
Non-medicated	4	84	75	0.24	−0.06, 0.54	
Adaptation Night						
No	6	227	139	0.18	−0.03, 0.40	0.04
Yes	4	74	62	0.14	−0.19, 0.48	
Stage 1						
<i>Total data set</i>	8	198	136	0.07	−0.14, 0.08	
Gender						
Male & female sample	4	124	74	0.06	−0.23, 0.35	0.005
Male only	4	74	62	0.08	−0.22, 0.37	
Average Age						
Younger than 9 years	4	143	72	0.35*	0.05, 0.64	6.82*
Older than 9 years	4	55	64	−0.21	−0.51, 0.09	
Control Group Screening						
Screened for ADHD	5	134	82	−0.13	−0.48, 0.23	2.37
Not screened/Not reported	3	64	54	0.34	−0.14, 0.82	
Medication						
Include medicated Ss	5	148	87	0.13	−0.15, 0.41	0.38
Non-medicated Ss	3	50	49	−0.005	−0.32, 0.31	
Adaptation Night						
No	4	124	74	0.06	−0.23, 0.35	0.005
Yes	4	74	62	0.08	−0.22, 0.37	
Stage 2						
<i>Total data set</i>	8	198	136	−0.06	−0.26, 0.15	
Gender						
Male & female sample	4	124	74	−0.26	−0.55, 0.03	3.85*
Male only	4	74	62	0.16	−0.14, 0.45	
Average age						
Younger than 9 years	4	143	72	−0.13	−0.43, 0.16	0.54
Older than 9 years	4	55	64	0.02	−0.27, 0.32	
Control group screening						
Screened for ADHD	5	134	82	−0.07	−0.33, 0.18	0.07
Not screened/Not reported	3	64	54	−0.02	−0.38, 0.35	
Medication						
Medicated	5	148	87	−0.23	−0.51, 0.04	3.57
Non-medicated	3	50	49	0.17	−0.14, 0.48	
Adaptation Night						
No	4	124	74	−0.26	−0.55, 0.03	3.85*
Yes	4	74	62	0.18	−0.14, 0.45	
SWS						
<i>Total data set</i>	11	315	211	−0.06	−0.22, 0.09	
Gender						
Male & female sample	7	241	149	−0.02	−0.20, 0.17	0.86
Male only	4	74	62	−0.17	−0.45, 0.10	
Average age						
Younger than 9 years	6	230	125	−0.08	−0.28, 0.11	0.11

Table 3 (continued)

	<i>k</i>	<i>n</i> ADHD	<i>n</i> Control	<i>d</i>	95% CI	<i>Q</i> [†]
Older than 9 years	5	85	86	-0.03	-0.29, 0.23	
Subjects recruitment						
General referrals	5	158	87	-0.17	-0.40, 0.06	1.92
Sleep clinic referrals	3	121	85	0.08	-0.20, 0.36	
Diagnosis						
No standard criteria	4	112	81	0.10	-0.16, 0.36	2.42
DSM	7	203	130	-0.15	-0.35, 0.04	
Comorbidity						
Excluded	6	163	99	-0.13	-0.32, 0.07	0.96
Included/not reported	5	152	112	0.03	-0.22, 0.28	
Medication						
Medicated	6	217	126	-0.08	-0.28, 0.11	0.09
Non-medicated	5	98	85	-0.03	-0.28, 0.22	
Adaptation night						
No	7	241	149	-0.02	-0.20, 0.17	0.86
Yes	4	74	62	-0.17	-0.45, 0.10	
REM						
<i>Total data set</i>	11	319	221	-0.04	-0.31, 0.23	
Gender						
Male & female sample	7	245	159	-0.11	-0.46, 0.23	0.55
Male only	4	74	62	0.11	-0.36, 0.58	
Average age						
Younger than 9 years	6	230	125	-0.22	-0.56, 0.11	2.40
Older than 9 years	5	89	96	0.17	-0.20, 0.53	
Subjects recruitment						
General referrals	4	144	77	-0.04	-0.55, 0.48	0.13
Sleep clinic referrals	3	121	85	-0.17	-0.73, 0.38	
Control group screening						
Screened for ADHD	8	255	167	-0.13	-0.44, 0.17	1.41
Not screened/Not reported	3	64	54	0.24	-0.29, 0.78	
Diagnosis						
No standard criteria	4	112	81	-0.25	-0.68, 0.17	1.52
DSM	7	207	140	0.08	-0.24, 0.40	
Comorbidity						
Excluded	6	163	99	-0.12	-0.50, 0.27	0.36
Included/not reported	5	156	122	0.05	-0.35, 0.46	
Medication						
Medicated	7	235	146	0.14	-0.18, 0.45	3.34
Non-medicated	4	84	75	-0.33	-0.73, 0.06	
Adaptation night						
No	7	245	159	-0.12	-0.33, 0.08	0.65
Yes	4	74	62	0.02	-0.27, 0.32	
REM Latency						
<i>Total data set</i>	10	285	189	0.02	-0.30, 0.33	
Gender						
Male & female sample	6	211	127	0.12	-0.28, 0.52	0.78
Male only	4	74	62	-0.18	-0.72, 0.36	
Average age						
Younger than 9 years	6	230	125	-0.09	-0.51, 0.33	0.62
Older than 9 years	4	55	64	0.18	-0.36, 0.72	
Control group screening						
Screened for ADHD	7	221	135	0.12	-0.26, 0.51	1.10
Not screened/Not reported	3	64	54	-0.26	-0.87, 0.35	
Diagnosis						
No standard criteria	4	112	81	-0.14	-0.66, 0.38	0.58
DSM	6	173	108	0.12	-0.32, 0.56	

Table 3 (continued)

	<i>k</i>	<i>n</i> ADHD	<i>n</i> Control	<i>d</i>	95% CI	<i>Q</i> [†]
Comorbidity						
Excluded	6	163	99	-0.07	-0.50, 0.37	0.31
Included/not reported	4	122	90	0.12	-0.38, 0.62	
Medication						
Medicated	6	201	114	-0.18	-0.58, 0.24	2.02
Non-medicated	4	84	75	0.29	-0.20, 0.79	
Adaptation Night						
No	6	211	127	0.12	-0.10, 0.34	1.57
Yes	4	74	62	-0.19	-0.50, 0.21	
AHI/RDI						
Total data set	5	227	132	0.10	-0.40, 0.60	
PLMS						
Total data set	7	258	159	0.26*	0.04, 0.49	
Average age						
Younger than 9 years	3	175	80	0.20	-0.07, 0.47	0.43
Older than 9 years	4	83	79	0.35*	0.02, 0.67	
Subjects recruitment						
General referrals	3	119	54	0.41*	0.06, 0.76	0.57
Sleep clinic referrals	3	121	85	0.24	-0.05, 0.52	
Diagnosis						
No standard criteria	2	87	53	0.14	-0.20, 0.48	0.73
DSM	5	171	106	0.33*	0.07, 0.59	
Arousals						
Total data set	6	161	128	-0.04	-0.25, 0.17	
Average age						
Younger than 9 years	3	117	75	-0.12	-0.37, 0.14	0.88
Older than 9 years	3	44	53	0.09	-0.25, 0.43	
Diagnosis						
No standard criteria	3	96	69	-0.15	-0.43, 0.13	1.19
DSM	3	65	59	0.08	-0.22, 0.38	
Medication						
Medicated	3	88	64	0.06	-0.28, 0.38	0.47
Non-medicated	3	73	64	-0.10	-0.36, 0.17	

* $p < 0.05$; ** $p < 0.01$.

K, number of studies included in the analysis; *d*, Cohen's standardized effect size statistic; *n* ADHD, number of participants with attention deficit hyperactivity disorder in the combined samples; *n* Control, number of control participants in the combined samples; ADHD, attention deficit hyperactivity disorder; PSG, polysomnography; AI, apnea index; AHI, apnea-hypopnea index; RDI, respiratory disturbance index; REM, rapid eye movement sleep; SWS, slow wave sleep; TST, total sleep time; CI, confidence interval.

[†]*Q* for comparison between subcategories of a moderator.

significantly differ on total sleep time, none of the effects is significant on its own right. Second, with regard to stage 1 sleep, where indeed younger samples of ADHD children showed more stage 1 sleep than control children without ADHD, fail-safe analysis reveals that only one additional study with null results is sufficient to reduce this effect to insignificance.

Gender

The combined effect size of total sleep time in samples that included only male participants

($d = 0.30$, $p < 0.05$, CI = 0.006, 0.60) was larger than the combined effect size of samples that included both males and females ($d = -0.17$, CI = -0.39, 0.04), $Q = 6.57$, $p < 0.05$. However, further analysis shows that only two additional studies with null results may be sufficient to reduce the total sleep time effect in male only samples to insignificance.

A significant modulation of time spent in stage 2 sleep by gender was also found. Although both the combined effects of samples containing only male participants ($d = 0.16$, CI = -0.14, 0.45) and of samples containing male and female participants ($d = -0.26$, CI = -0.55, 0.03) were non-significant,

the difference between the two was, $Q = 3.85$, $p < 0.05$.

Comorbidity

Sleep latency was longer in children with ADHD relative to controls in samples where children with comorbid conditions were excluded ($d = 0.37$, $p < 0.05$, $CI = 0.11, 0.62$). In contrast, in samples that included children with comorbidity the combined effect size was not-significant ($d = -0.03$, $CI = -0.29, 0.23$), with a significant difference between the two types of samples $Q = 4.96$, $p < 0.05$. Fail-safe number for the combined effect found for samples excluding comorbid condition was 7, again a very low number by methods described in the literature.

Adaptation nights

The results of the meta-analysis revealed a number of effects related to studies that did or did not include adaptation night (i.e., performed PSG on more than one night).

Total sleep time was longer in children with ADHD in comparison to controls in studies that included an adaptation night ($d = 0.30$, $p < 0.05$, $CI = 0.006, 0.60$); this was not the case in studies with no adaptation night ($d = -0.18$, $CI = -0.39, 0.04$); $Q = 6.57$, $p < 0.01$.

With regard to stage 2 sleep in studies that have used an adaptation night, children with ADHD had longer stage 2 sleep than controls ($d = 0.18$, $CI = -0.14, 0.45$); whereas in studies with no adaptation nights children with ADHD had shorter stage 2 sleep ($d = -0.26$, $CI = -0.55, 0.03$). While each of these combined effect sizes was not statistically significant, the difference between the combined effects was, $Q = 3.85$, $p < 0.05$.

Conclusions

Our study is the first meta-analysis on sleep in children with ADHD that include evaluation of major potential moderating factors. Before addressing the specific findings, the limitations of this meta-analysis should be highlighted. The power of our meta-analysis was limited by the small number of studies that met our inclusion criteria. This limited number of studies results from the small number of PSG studies in children in general and from the fact that some studies in the field have basic methodological flaws that were considered unacceptable for inclusion in the meta-analysis.

Furthermore, some major factors such as ADHD subtypes and specific comorbid conditions could not be assessed because there were not enough studies that systematically documented these factors.

Notwithstanding these limitations, the results of our analysis provide some support for specific characteristics of sleep in children with ADHD and dismiss some of the claims related to non-consistent findings in the literature. Our meta-analysis revealed that the only significant main difference between children with ADHD and controls is in the prevalence of PLMS. Children with ADHD are more likely to have PLMD or increased number of PLMS. Although this finding in itself is not very robust, it did cross the threshold of a significant combined effect across studies. The fact that this effect is somewhat stronger in studies with a DSM-based diagnosis and in studies with referrals from the general population provide some additional support to this finding. Additional studies on PLMS with better experimental control have the potential to further consolidate the links between PLMS and ADHD.

Our finding of increased prevalence of PLMS/RLS in children with ADHD lends support to the growing literature on this topic (e.g., Refs.^{31–34}). However, the multifactor etiology of ADHD and the fact that most children with ADHD do not have significant PLMD suggest that PLMD could not be considered as a major causal factor in this disorder.⁶

Age appears to be a significant moderator in the analysis of the associations between sleep and ADHD. Although, our analysis was limited to the average age of the samples, we found distinct differences between studies with younger versus older samples. Younger children with ADHD tended to have shorter sleep than controls whereas the opposite was true for older children. These results may reflect some changes associated with distinct maturational patterns of sleep need, with increased sleep need or sleep debt in older children with ADHD. Significant results were also obtained with regard to stage 1 sleep. Considering the maturational changes in the clinical picture of ADHD^{13,14,17} and the maturational changes in sleep (e.g., Refs.^{35–41}), these findings should guide future research. Performing studies with large samples that include age (or age groups) as a potential moderator should be preferred. Alternatively, researchers may wish to use narrower age groups that would limit the confounding maturational effects.

Our ability to assess the role of gender was limited by the fact that most studies did not include girls or included only a small number of girls. The

results of these studies were not reported separately for boys and girls and therefore the only possible comparison was between studies that did or did not include girls. The results provide some indication that in samples that included males only, children with ADHD had increased total sleep time, where the opposite tendency was noted in samples that included boys and girls. Similar tendencies were found for stage 2 sleep. Because of the significance of gender in sleep maturation^{37,41} and in ADHD,^{13,14,18} future studies should address the role of gender as a possible moderator of the relationships between sleep and ADHD.

Comorbidity, another major conceptual and methodological issue in the ADHD literature, appears to play some role in the relationships between sleep and ADHD. Our findings suggest that when children with comorbid conditions (mood and anxiety disorders) were not included in the ADHD sample, sleep latency was longer in children with ADHD than in controls. It is important to emphasize that children with conduct disorders and learning disorders were not excluded under the comorbidity criteria. This finding may suggest that children with ADHD have more difficulty falling asleep in the laboratory. However, there are different alternative explanations for this finding. It may suggest that children with ADHD have more difficulty falling asleep in general, it could be a result of their difficulty adjusting to laboratory settings and the bedtime imposed on them, or that they have a sleep schedule problem that makes it harder for them to fall asleep at a time not adjusted to their biological clock.^{1,42} These results are also compatible with the findings of unstable bedtime in children with ADHD.^{43,44} These findings on the role of comorbidity should be considered with caution because of the methodological limitations in assessing this factor and they should serve as an indication on the importance of assessing and controlling for comorbidity in future studies.

The last moderator that appears to affect the association between ADHD and sleep was the inclusion of an adaptation night. Although the findings on "first night effects" in children are not straightforward,^{45,46} it has been demonstrated in adults and children that when studied in a sleep laboratory, participants may present signs of stress or adjustment difficulties which are manifested in distinct sleep characteristics (e.g., longer sleep latency, lower sleep efficiency) on the first night in comparison to the following nights.^{45,47} The results of our meta-analysis suggest that the non-inclusion of an adaptation night may compromise the findings of studies on sleep stages in children with ADHD. We found that in studies that included an adapta-

tion night total sleep time was longer in children with ADHD in comparison to controls. Similar results were found with regard to stage 2 sleep. It has been suggested that participants with distinct psychopathology or personality characteristics have different first-night effect.^{48,49} Therefore, the first-night effect may play a masking role in the study of sleep in ADHD. Future studies should use at least one adaptation night and compare the findings on adaptation night and on subsequent non-adaptation nights.

It is important to note that it is possible that lack of consistent findings in specific areas of evaluation do not necessarily reflect lack of underlying relationships between sleep-related phenomena and ADHD. For instance, the lack of consistent findings with regard to sleep apnea may reflect the fact that there are wide variations in the ways that apneas and hypoapneas are defined and measured in children.⁷ It is possible, that with standardized and appropriate definitions and measures of sleep apnea or airways resistance in children, more consistent differences between children with ADHD and controls would emerge.

In conclusion, our meta-analysis reveals that the research on sleep in children with ADHD has been severely compromised by conceptual and methodological problems associated with the definition and diagnosis of ADHD and many related confounding factors. The results lend support to the hypothesis on increased prevalence of PLMS in children with ADHD. This could be an underlying or an exacerbating factor in the symptoms of some children diagnosed with ADHD. Studies on sleep and neurobehavioral functioning have indicated that fragmented or restricted sleep could lead to neurobehavioral deficits that are associated with ADHD.^{33,50-52} Furthermore, clinical practice has demonstrated that primary sleep disorders could be manifested or misdiagnosed as ADHD in some children.^{53,54} Therefore, from a clinical perspective, the assessment of sleep remains a crucial component in the evaluation and diagnosis of ADHD. When sleep experts diagnose a child with a primary sleep disorder they should alert the parents and other clinicians to the possibility that this disorder may have serious consequences in related functional domains, and particularly in the area of attention and behavior regulation that is associated with ADHD.

From research perspective, we believe that additional small PSG studies on children with and without ADHD would not have substantial contribution in clarifying the empirical picture. We believe that a large-scale study, probably a multi-site effort, which would take into account the major

moderators and the guidelines proposed here, may contribute to elucidate the elusive associations between sleep and ADHD.

Research agenda

There is a need for large-scale studies on sleep in children with ADHD that would adhere to the following guidelines:

- Use standardized diagnostic system (e.g., DSM-IV) with corroboration by multiple sources of information (e.g., parents and teachers).
- Recruit children with ADHD from psychiatric clinics or from the general population and refrain from using convenient samples of children referred to a sleep clinic.
- Screen control groups for possible inclusion of children with undiagnosed ADHD.
- Assess comorbidity either as an exclusion criteria or as a moderating factor.
- Consider groupings based on ADHD subtypes (e.g., attention deficit vs. hyperactive or combined types).
- Include males and females with ADHD and use gender as a moderating factor.
- Consider age as a potential moderating factor.
- Study more than one night of PSG because clinical and control groups may have different first night effect.
- Control for medication use and/or include washout period.

Practice points

Our review suggests that children with ADHD tend to have more PLMS or PLMD. This may be an underlying or exacerbating factor in the clinical picture of some children with ADHD. Other sleep disorders as well as insufficient sleep may play a role in some children with ADHD even if these disorders are not more prevalent in children with ADHD. Therefore, when a major sleep disorder is diagnosed in children, clinicians should be alerted to the potential negative impact on the child's functioning including the existence of ADHD-like symptoms. During the diagnostic procedures of children suspected for ADHD special attention should be given to possible underlying involvement of sleep disorders or insufficient sleep.

Acknowledgment

The authors are thankful to Ornit Arbel for her help in preparing this manuscript.

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