REVIEW

Sleep disorders in patients with ADHD: impact and management challenges

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Abstract: Attention deficit/hyperactivity disorder (ADHD) is one of the most commonly diagnosed disorders in childhood, enduring through adolescence and adulthood and presenting with symptoms of inattention, hyperactivity, and/or impulsivity and significantly impairing functioning. Primary sleep disorders such as sleep-disordered breathing, restless leg syndrome, circadian rhythm sleep disorder, insomnia, and narcolepsy are commonly comorbid in these individuals but not often assessed and are therefore often left untreated. Sleep disturbances in individuals with ADHD can result in significant functional impairments that affect mood, attention, behavior, and ultimately school/work performance and quality of life. Previous reviews have described findings related to sleep but have neglected to examine potential impacts of these sleep disorders and ADHD on daytime functioning. This review investigates empirical findings pertaining to sleep abnormalities and related cognitive, behavioral, emotional, and physical impairments in individuals with ADHD and comorbid primary sleep disorders across the life span. It discusses implications to management and highlights existing limitations and recommended future directions.

Keywords: ADHD, impairments, sleep-disordered breathing, restless leg syndrome, circadian rhythm sleep disorders, insomnia, narcolepsy

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most commonly diagnosed disorders in childhood and adulthood. It affects approximately 3%–5% of youth[1] and 2.9% of adults.[2] It endures throughout adolescence and adulthood. A diagnosis of ADHD is dependent on developmentally inappropriate symptoms of inattention, hyperactivity, and/or impulsivity, with onset before the age of 12 years and impaired functioning in two or more settings. If untreated, individuals with ADHD struggle with impairments across many crucial domains of functioning, including academic, occupational, and social realms.[3]

In clinical practice, sleep problems are reported in an estimated 25%–50% of individuals who have ADHD,[4–6] and adults who do not get the recommended amount of sleep are more likely to report ADHD symptoms.[7] Sleep disturbances in such individuals have been associated with comorbid primary sleep issues and/or alterations associated with the medications used to treat ADHD.[8] In an affected individual, sleep disturbances that result in sleep restriction or sleep fragmentation can lead to excessive daytime fatigue and interfere with mood, attention, behavior, and physical health, all of which are critical for school/work performance and a good quality of life. However, although sleep problems are very common in individuals with ADHD, comorbid sleep

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disorders are often overlooked and left untreated in ADHD populations.

Researchers have examined the associations between ADHD and sleep-disordered breathing (SDB), restless leg syndrome (RLS), circadian rhythm sleep disorders (CRSDs), insomnia, and narcolepsy.[9–11] SDB is characterized by abnormal patterns of respiration and/or ventilation during sleep,[12] while obstructive sleep apnea (OSA) is characterized by partial or complete upper airway obstruction, leading to disrupted sleep.[13,14] A history of snoring or possible OSA during childhood is associated with a twofold difference in the odds of ADHD diagnosis or symptoms,[15,16] and elevated incidence of SDB is found among individuals with ADHD.[17–21] SDB affects psychological outcomes through various mechanisms, including the deleterious effects of hypoxic insults and the resulting stress/inflammation in the brain and/or repeated arousal-based sleep disruptions.[22] These mechanisms can alter the neurochemical substrates of the prefrontal cortex[23] leading to neurobehavioral deficits underlying ADHD symptoms.

RLS is a common sensorimotor disorder characterized by an irresistible urge to move the legs, often accompanied by uncomfortable sensations in the legs or (less frequently) other body parts. These sensations are worse at rest, relieved by movement, and most bothersome in the evening or night. Patients frequently experience insomnia from leg discomfort and the need to move around. Dopaminergic abnormalities and iron deficiency are presumed to underlie this comorbidity.[24–31] Although the prevalence of RLS in the pediatric population is unknown, approximately 10% of adults in the USA have the disorder. The evidence suggests that up to 44% of individuals with ADHD have RLS or RLS-like symptoms and up to 26% of individuals who have RLS have ADHD or ADHD-like symptoms.[28,30,32–35] The underlying pathophysiology linking RLS and ADHD may lie in the deficit of dopamine in the nigrostriatal brain region, which has been associated with both disorders.[36] In addition, iron deficiency has also been linked to ADHD and RLS,[37] since iron is a cofactor for tyrosine hydroxylase, the rate-limiting enzyme responsible for dopamine synthesis, which also influences the dopamine pathway directly. Sleep disruption itself may lead to symptoms of ADHD, and daytime symptoms of RLS such as restlessness and inattention may mimic ADHD symptoms.[38]

CRSDs involve a problem in the timing when a person sleeps and is awake. They are caused by alterations of the circadian time-keeping system or its entrainment mechanisms or by a misalignment of the endogenous circadian rhythm and the external environment. Delayed sleep phase syndrome (DSPS) occurs when a person regularly goes to sleep and wakes up >2 hours later than is considered normal. Individuals with ADHD have been found to have changes in these mechanisms, decreases in the volume of the pineal gland, and/or clock gene abnormalities; in particular, a recent study conducted by Baird et al found that the expression of clock genes *BMAL1* and *PER2* was altered in individuals with ADHD.[39] DSPS and late chronotype are frequently comorbid in adults[3,40,41] and adolescents[42] with ADHD. The pathophysiology linking ADHD and CRSD maybe both behavioral and biological.[43] Deficits in impulsivity control may affect the ability of an individual to settle down, leading to bedtime resistance and resulting in delayed sleep onset. In addition, it is proposed that individuals with ADHD may have a stronger circadian evening preference and possible endogenous melatonin increase delay.[43,44]

Insomnia is a sleep disorder characterized by difficulty falling or staying asleep, even when a person has the chance to do so.[45] Prolonged sleep onset, delayed bedtime, and frequent night awakenings are commonly seen in individuals with ADHD. It is more frequent among children (73.3%)[46] and adults with ADHD (66.8%)[47] than in the general population (children: 20%–30%;[48] adults: 6%–50%[49,50]). Unhealthy sleep practices and a lack of routines, especially at bedtime, have been shown to be more common in individuals with ADHD and to have a significant negative impact on sleep initiation.[51] In addition, these sleep issues could result from increased resistance at bedtime, difficulty in settling down in the evening, or poor sleep hygiene.

Narcolepsy is a chronic neurological disease that manifests as difficulty with maintaining continuous wake and sleep. The clinical presentation varies, but a diagnosis of narcolepsy requires excessive daytime sleepiness (EDS) occurring alone or together with features of rapid eye movement (REM), sleep dissociation (eg, cataplexy, hypnagogic/hypnopompic hallucinations, sleep paralysis), and disrupted nighttime sleep. There are two major types of narcolepsy: type 1 narcolepsy diagnosis is based on the individual either having low levels of hypocretin or reporting cataplexy and having EDS; type 2 narcolepsy diagnosis involves EDS in the absence of cataplexy and with normal hypocretin levels.[45] Retrospectively, adults with narcolepsy were found to have a twofold greater likelihood of having a childhood diagnosis of ADHD compared with controls.[52] In addition, evidence suggests that children with ADHD experience hypoarousal and that their hyperactive/impulsive symptoms may be compensatory behaviors for fatigue.[53] The link between ADHD

and narcolepsy is poorly understood,[11] but it is hypothesized that EDS in individuals with narcolepsy could result in inattention, poor executive function, and impulse control problems that mimic ADHD and respond well to stimulant medication.[54–56] Ultimately, the overlap of symptoms of ADHD and narcolepsy may lead to diagnostic confusion or misdiagnosis of the disorders.[54] Another hypothesis is that the link may lie in a shared brain pathophysiology.[57] In ADHD, a suspected dysregulation of dopamine and noradrenaline is an accepted hypothesis,[58] and REM sleep, in turn, is affected by noradrenergic and cholinergic neurons.[59] Dysregulation of noradrenaline could lead to changes in REM sleep similar to that seen in patients with narcolepsy.[57] In addition, medication geared at treating ADHD targets the abovementioned neurotransmitters,[60] and there is an overlap with medication used to treat narcolepsy.[61,62] There may also be a possible genetic link between narcolepsy and ADHD. Individuals with ADHD and hypersomnia can have shorter REM latencies and fulfill the criteria for type 2 narcolepsy.[57] In addition, these individuals tend to have an absence of the DQB1*06:02 allele that is usually found in individuals with type 1 narcolepsy and some individuals with type 2 narcolepsy without ADHD, alluding to the possibility that individuals with ADHD and hypersomnia could be part of a subtype of type 2 narcolepsy.[57]

Previous reviews have described research findings pertaining to sleep and the mechanisms that may underlie the comorbidity between the abovedescribed primary sleep disorders and ADHD.[63] However, the existing reviews have neglected to examine the potential impacts of these disorders on the daytime functioning of individuals who present with ADHD and sleep issues.[64–66] This is a problem because in order to provide optimal care, clinicians need to be aware of sleep problems among patients with ADHD and their potential impacts on the very symptoms they are attempting to treat and manage. An investigation of how sleep disturbances impact ADHD symptoms will help clarify the outcomes and management challenges associated with treating individuals with ADHD and comorbid primary sleep disorders. Hence, the goal of the present review is to describe empirical findings pertaining to sleep abnormalities and cognitive, behavioral, emotional, or physical outcomes associated with sleep issues in individuals with ADHD and comorbid primary sleep disorders.

Methods

We employed a narrative review methodology to identify and synthesize empirical studies that have examined the sleep patterns of individuals with ADHD and each of the primary sleep disorders known to be comorbid with ADHD, namely SDB, RLS, CRSD, insomnia, and narcolepsy. Three electronic databases were searched in July 2018 (Embase, MEDLINE, and PsycINFO) for studies published in the prior 5 years (between January 1, 2013 and July 1, 2018). Additional records were identified by searching the references of the selected original research papers and review articles.

Separate parallel searches were conducted for each primary sleep disorder using the following key words: ADHD *and* narcolepsy; ADHD *and* CRSD, dim light melatonin onset, light therapy, *or* melatonin; ADHD *and* restless leg syndrome, RLS, periodic *and* extremities, periodic limb movement, iron, ferritin, ferritins, levodopa, *or* L-DOPA; ADHD *and* sleep apnea *or* sleep-disordered breathing; and ADHD *and* insomnia. The inclusion criteria were: 1) peer-reviewed original research of subjects with a sleep disorder or ADHD, in which variables related to both ADHD and sleep were measured; and 2) studies that were written in the English language and used quantitative methods. All the included published empirical studies are listed in the summary table (see Table 1). In total, the literature search yielded 39 relevant papers, including thirteen, seven, eight, seven, and six for ADHD and SDB, RLS, CRSDs, insomnia, and narcolepsy, respectively.

Results

In the following sections, findings based on recent empirical data on the sleep characteristics and their associations with daytime functioning and physical health of individuals with ADHD primary sleep disorders are reviewed. These results are organized separately for each of these subgroups in the following way: findings regarding sleep, sleepiness, or circadian characteristics are subdivided according the nature of the tools that were used (objective or subjective measures) and the age groups of the participants. Daytime impairments are divided into cognitive, emotional, and physical outcomes. Detailed information for each study referenced can be found in Table 1.

ADHD and SDB

The present review includes 13 studies (six cross-sectional, two case–control, one retrospective cohort, two prospective cohort, and two open-label) that examined the sleep characteristics of individuals with SDB and ADHD.

Sleep characteristics[67–76]
Polysomnography (PSG)
School-age children. N/A; Adolescents. N/A; Adults. No significant differences in apnea–hypopnea index, a measure

Table 1 Summary of studies reviewed

Author and year	Sample	Study design	Diagnoses	Measures
Table 1.1 OSA and sleep-disordered breathing				
Smith et al (2017)[67]	631 children Sex: 347 males, 284 females Age (mean ± SD), years: 6.94±1.30	Cross-sectional	ADHD: CPRS-R, CBCL OSA/SDB: PSG	Sleep: PSG Attention: CPRS-R, CBCL Cognitive: NEPSY, NEPSY-II Intelligence: DAS
Kim et al (2018)[68]	170 children with AT, 150 healthy controls Sex: 182 males, 135 females Age (mean ± SD), years: OSA/SDB: 7.7±1.5; controls: 7.6±1.5	Prospective cohort intervention: AT	ADHD: SDQ OSA/SDB: PSG, SRBD	Sleep: PSG, SRBD Attention: SDQ Socioemotional: CDI SCARED Physical: BMI
Wu et al (2017)[80]	437 children with OSA Sex: 298 males, 139 females Age (mean ± SD), years: 5.71±1.45	Retrospective cohort	ADHD: DSM-IV criteria OSA/SDB: PSG	Sleep: OSA-18 Socioemotional: OSA-18 Physical: OSA-18
Smith et al (2016)[69]	1,022 children Sex: 562 males, 460 females Age (mean ± SD), years: 6.86±0.89	Cross-sectional	ADHD: CPRS-R, CBCL OSA/SDB: PSG Parental report	Sleep: PSG Attention: CPRS-R, CBCL
Smith et al (2017)[67]	1,116 children Sex: 598 males, 518 females Age (mean ± SD), years: 6.84±0.86	Cross-sectional	ADHD: CPRS-R OSA/SDB: PSG	Sleep: PSG Attention: CPRS-R, CBCL, NEPSY, NEPSY-II
Villa et al (2016)[71]	76 children with suspected OSA Sex: 44 males, 32 females Age (mean ± SD), years: 4.95±1.75	Open-label trial intervention: AT, RME, or medical therapy	ADHD: DSM-IV criteria OSA/SDB: PSG Medical history	Sleep: PSG Attention: unspecified DSM-IV symptom checklist
Zhu et al (2014)[72]	51 children with OSA Sex: 35 males, 16 females Age (mean ± SD), years: 7.68±2.15	Open-label trial intervention: AT	ADHD: IVA-CPT OSA/SDB: PSG	Sleep: PSG Attention: IVA-CPT

Sleep differences	Daytime impairments			Conclusions
	Cognitive	Emotional	Physical	
N/A	Snorers vs nonsnorers: more ADHD symptoms. Higher AHI was associated with less hyperactivity and inattention symptoms. Increased snoring, but not AHI, was associated with worse performance on cognitive tests.	Snorers vs nonsnorers: more internalizing and externalizing problems.	N/A	Snoring, but not AHI, was associated with more daytime dysfunction in attention, cognition, and psychological aspects.
AT improved SDB symptoms	AT reduced hyperactivity and inattention symptoms. This improvement was reduced in older children (vs younger) and obese children (vs normal weight).	AT reduced symptoms of anxiety and depression.	AT increased odds of being overweight.	AT improved symptoms of SDB and daytime symptoms of ADHD, depression, and anxiety. Young children with normal weight had better improvement.
OSA + ADHD vs OSA: more sleep disturbances, higher AHI, and lower oxygen saturation.	OSA + ADHD vs OSA: more daytime problems.	OSA + ADHD vs OSA: greater emotional distress and caretaker concern.	OSA + ADHD vs OSA: more physical suffering	OSA with comorbid ADHD had worse daytime functioning across cognitive, emotional, and physical outcomes compared with OSA without ADHD.
N/A	Snorers with normal AHI vs nonsnorers with normal AHI: worse CPRS-R. Snorers with normal AHI vs nonsnorers with normal AHI, mild AHI, severe AHI: higher hyperactivity and ADHD scores on the CBCL.	Snorer with normal AHI vs nonsnorers with normal AHI: worse internalizing.	N/A	Snoring with a normal AHI is associated with worse daytime functioning for ADHD and internalizing than either snorers with abnormal AHI or nonsnorers with normal AHI.
N/A	SDB is associated with behavioral problems. SDB was not directly associated with cognitive problems. However, behavioral problems were an indirect mediator of the association between SDB and cognitive problems.	N/A	N/A	SDB is associated with more behavioral problems, which may lead to cognitive problems.
AHI improved after AT and RME. Mean O_2 saturation improved in AT group.	AT improved ADHD symptoms.	N/A	N/A	AT was better at improving symptoms of ADHD than RME or medical therapy.
AHI and mean O_2 saturation improved between baseline and 3 months follow-up, as well as between 3 and 6 months follow-up. Those with severe OSA had worse parameters at baseline, but at 6 months follow-up there were no differences based on initial severity.	IVA-CPT scores improved from baseline to 3 months follow-up, as well as from 3 to 6 months follow-up. Severity of OSAHS was associated with worse Full Attention Quotient scores, but not Hyperactivity or Full Scale Response Control Quotient.	N/A	N/A	AT improved performance on a cognitive test of attention. Performance continued to improve until at least 6 months follow-up.

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Table 1 (*Continued*)

Author and year	Sample	Study design	Diagnoses	Measures
Vitelli et al (2015)[73]	36 children with OSA, 38 children with OSA + obesity, 58 controls Sex: 77 males, 57 females Age (mean ± SD), years: OSA: 8.29±2.04; OSA + obesity: 8.73±1.69; controls: 8.89±1.62	Case–control	ADHD: ADHD-RS OSA/SDB: PSG	Sleep: PSG Attention: ADHD-RS Physical: BMI
Oğuztürk et al (2013)[74]	81 treatment-naïve adults with OSA, 32 controls Sex: 89 males, 27 females Age (mean ± SD), years: OSA: 48.1±8.9; controls: 44.1±13.2	Case–control	ADHD: ASRS OSA/SDB: PSG	Sleep: PSG Sleepiness: ESS Attention: ASRS Socioemotional: HADS Physical: SF-36
Perfect et al (2013)[75]	263 children Sex: 123 males, 140 females Age (mean ± SD), years: 13.22±1.70	Prospective cohort	ADHD: medical history OSA/SDB: PSG Parent-reported snoring	Sleep: PSG SHQ Attention: BASC-2 Socioemotional: ABAS-II School problems parent report
Ekici et al (2013)[76]	90 adult snorers or with OSA Sex: 67 males, 23 females Age (mean ± SD), years: 44.23±10.23	Cross-sectional	ADHD: ASRS OSA/SDB: PSG	Sleep: PSG Attention: ASRS
Amiri et al (2015)[78]	53 post-AT children with untreated ADHD Sex: 28 males, 25 females Age (mean ± SD), years: 6.89±2.06	Prospective cohort intervention: AT	ADHD: K-SADS-PL OSA/SDB: direct observation of tonsils and medical history	Attention: CPRS-R
Table 1.2 RLS and periodic limb movement disorder				
Roy et al (2018)[86]	1,632 adults Sex: 757 males, 875 females Age (mean ± SD), years: 43.2±12.7	Cross-sectional	ADHD: ADHD-RS RLS: IRLSSG criteria	Sleep: JSS Attention: ADHD-RS, WURS-K
Um et al (2016)[82]	28 children with ADHD Sex: 22 males, 6 females Age (mean ± SD), years: male: 8.95±2.26; female: 9.17±2.04	Cross-sectional	ADHD: DSM-IV-TR criteria PLMD: PSG	Sleep: PSG Attention: CGI-P Cognitive: MFFT-KC Intelligence: K-WISC-III

Sleep differences	Daytime impairments			Conclusions
	Cognitive	Emotional	Physical	
N/A	OSA + Obesity vs OSA: more symptoms of ADHD.	N/A	N/A	In children with OSA, obesity is associated with greater symptoms of ADHD (vs normal weight).
OSA + ADHD vs OSA: higher sleepiness, no PSG differences.	OSA vs controls: no differences in ADHD prevalence.	OSA + ADHD vs OSA: more anxiety and depression symptoms.	OSA + ADHD vs OSA: lower physical health quality of life, no difference in BMI	OSA with comorbid ADHD has worse emotional and physical outcomes than OSA without ADHD.
N/A	Persistent SDB vs never SDB: no significant differences in ADHD diagnosis, greater hyperactivity, and lower school grades.	Persistent SDB vs never SDB: impaired social and communication skills.	N/A	Presence of current SDB and persistence of SDB are associated with increased hyperactivity symptoms, impaired social skills, and lower school grades.
N/A	Snoring vs OSA: no difference in ADHD symptoms.	N/A	N/A	No difference was found in cognitive outcomes between snorers and OSA adults.
N/A	AT improved ADHD symptoms between baseline and 3 months follow-up, as well as between 3 months follow-up and 6 months follow-up.	N/A	N/A	AT improved symptoms of ADHD and symptoms continue to improve at least until 6 months after surgery.
Adult ADHD is associated with increased odds of presenter RLS, OR = 4.73. After controlling for sleep disturbances, this association was no longer significant, which suggests that sleep disturbances may partially mediate the relationship between ADHD and RLS.	RLS vs non-RLS: prevalence of ADHD is 17.3% vs 4.2%.	N/A	N/A	The prevalence of RLS is higher in adults with ADHD.
Limb movement index: 11.64±3.90. Limb movement index with arousal: 6.74±2.33. Periodic limb movement: 0.30±1.57. Periodic limb movement with arousal: 0.05±0.25.	Higher limb movement index with arousal was associated with worse verbal IQ and number of correct answers in the MFFT-KC.	N/A	N/A	In children with ADHD, more symptoms of PLMD are associated with reduced performance on intelligence and cognitive tests.

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Table 1 (*Continued*)

Author and year	Sample	Study design	Diagnoses	Measures
Ghorayeb et al (2017)[87]	105 adults with RLS Sex: 43 males, 62 females Age (mean ± SD), years: 41.75±19.2	Cross-sectional	ADHD: ASRS RLS: IRLSSG	RLS: serum ferritin and iron. Attention: ASRS Socioemotional: MOCI
Ferri et al (2013)[83]	18 children with ADHD, 17 health controls Sex: 20 males, 15 females Age (mean ± SD), years: ADHD: 8.9±1.35; control: 9.4±2.0	Double-blind, placebo-controlled randomized clinical trial Intervention: 25 mg/100 mg of carbidopa and levodopa, increased up to 250–600 mg of levodopa vs placebo for the ADHD group	ADHD: DISC-IV RLS: PSG	Sleep: PSG
Akinci et al (2015)[84]	28 children with ADHD and 15 healthy controls Sex: 29 males, 14 females Age (median [age range]), years: ADHD: 10 (9–13); control: 10 (8–12)	Case–control	ADHD: K-SADS RLS: PSG	Sleep: PSG, PSQI Sleepiness: ESS
Garbazza et al (2018)[85]	15 ADHD adults without RLS/PLMD and 18 healthy controls Sex: 14 males, 19 females Age (mean ± SD), years: ADHD: 33.9±7.9; controls: 35.8±7.5	Case–control	ADHD: DSM-IV criteria RLS: RLDI	Sleep: PSG
Table 1.3 Circadian rhythm sleep disorders				
Bijlenga et al (2013)[91]	12 medication naïve adults with ADHD and DSPS, 12 healthy controls Sex: 12 males, 12 females Age (M±SD), years: ADHD + DSPS: 32.5±9.9; control: 32.4±10.8	Case–control	ADHD: DIVA 2.0 DSPS: inability to fall asleep at preferred time before 23:30 in the past 6 months	Sleep: MCTQ, SHQ, actigraphy Circadian rhythms: DLMO, CBT, actigraphy

Sleep differences	Daytime impairments			Conclusions
	Cognitive	**Emotional**	**Physical**	
RLS + ADHD vs RLS: no difference in serum ferritin and iron levels.	27.6% of patients with RLS have comorbid ADHD.	RLS + ADHD vs RLS: prevalence of OCD is 7.62% for both groups.	N/A	ADHD is highly comorbid with RLS. OCD comorbidity may also be higher in those with RLS.
ADHD vs control: higher PLMD index and lower periodicity of leg movements. No changes with treatment in periodicity of movement.	N/A	N/A	N/A	Children with ADHD had more PLMD symptoms than controls. Treatment with levodopa and carbidopa did not change RLS symptoms.
ADHD vs control: PLMI was higher. No differences in subjective perception of RLS.	N/A	N/A	N/A	RLS is greater in children with ADHD than in healthy children.
ADHD vs control: longer sleep latency, longer duration of periodic leg movements during sleep, and higher PLMS index in REM sleep.	N/A	N/A	N/A	Adults with ADHD but without RLS/PLMD present, greater subthreshold PLMD symptoms than healthy controls.
Sleep: ADHD + DSPS vs controls: midpoint of sleep was 1:52 hours later, bed time was 2:23 hours later, sleep start time was 2:20 hours later, sleep duration was 1:08 hours shorter on work days, sleep hygiene was worse, sleep efficiency was better by 4.5 percentage points. Circadian rhythms: ADHD + DPSP vs controls: DLMO onset occurred 1:23 hours later; 24-hour activity parameters were delayed. CBT and distal skin temperature were lower, while proximal skin temperature was higher.	N/A	N/A	N/A	Circadian rhythms of melatonin and activity were delayed in participants with ADHD and DSPS.

(*Continued*)

Table 1 (*Continued*)

Author and year	Sample	Study design	Diagnoses	Measures
Durmuş et al (2017)[92]	52 children with ADHD, 52 healthy controls Sex: 82 males, 22 females Age (M±SD), years: ADHD: 9.24±1.94; control: 9.20±1.20	Case–control	ADHD: K-SADS-PL Sleep: None	Sleep: CHSQ Chronotype: CCTQ Attention: CPRS, CTRS, DSM-IV symptom checklist. Intelligence: WISC-R
Snitselaar et al (2013)[90]	10 adults with ADHD Sex: 8 males, 2 females Age (mean ± SD), years: 33.2±7.6	Open-label trial Treatment: MPH	ADHD: DSM-IV criteria Sleep: None	Chronotype: MCTQ, DLMO Attention: ADHD-RS
Büber et al (2016)[88]	27 children and adolescents with ADHD and 28 healthy controls. Sex: 44 males, 11 females Age (mean ± SD), years: ADHD: 9.37±2.69; control: 10.50±2.71	Case–control	ADHD: K-SADS-PL Sleep: None	Chronotype: urinary 6-OH MS Attention: CPRS
Bron et al (2016)[40]	2,090 adults Sex: 696 males, 1,394 females Age (mean ± SD), years: lifetime depression or anxiety + ADHD: 47.6±11.3; lifetime depression or anxiety: 44.6±12.8; controls: 44.0±14.6	Cross-sectional	ADHD: CAARS DSPS: MCTQ	Chronotype: MCTQ Attention: CAARS Socioemotional: CIDI Physical: BMI
Bumb et al (2016)[95]	74 adults with ADHD, 86 healthy controls. Sex: 82 males, 78 females Age (mean ± SD), years: ADHD: 32.7±8.1; control: 23.1±2.6	Case–control	ADHD: ADHD-DC Sleep: none	Chronotype: MEQ Attention: ADHD-DC, WURS-K Intelligence: MWT-B
Molina-Carballo et al (2013)[89]	136 children with ADHD group, 42 healthy controls. Sex: 136 males, 42 females Age (mean ± SD), years: 9.70±2.55	Quasiexperimental open-label trial Intervention: extended release MPH	ADHD: DSM-IV or ICD-9 criteria Sleep: none	Sleep: sleep diary Attention: EDAH Chronotype: urinary 6-OH MS Serum melatonin Socioemotional: CDI Serum serotonin

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	Cognitive	Emotional	Physical	
ADHD vs control: more eveningness and worse sleep hygiene. In the ADHD group, eveningness was associated with the following subscales in the CSHQ: resistance to sleep, respiratory problems, daytime sleepiness, and total score. In the control group, eveningness was only associated with daytime sleepiness.	In the ADHD group, somatic symptoms in the CPRS were associated with eveningness. ADHD vs control: lower WISC-R scores.	N/A	N/A	Children with ADHD had greater eveningness, which was associated with worse sleep hygiene. Eveningness was associated with worse daytime somatic symptoms of ADHD.
Circadian rhythms: MPH increased melatonin levels but did not change the timing of DLMO.	Morningness was associated with greater reduction of symptoms after MPH treatment.	N/A		Patients with a morning type may have more improvement in ADHD symptoms than those with the evening type.
Circadian rhythms: ADHD vs control: higher levels of daytime, nighttime, and 24-hour melatonin.	Levels of 6-OH MS were not associated with symptom severity.	N/A	N/A	While melatonin levels are associated with the presence of ADHD, no evidence suggests that it was associated with daytime symptom severity or subtype.
Lifetime depression or anxiety + ADHD vs controls or lifetime depression or anxiety: shorter sleep duration (OR=2.8). Lifetime depression or anxiety + ADHD vs lifetime depression or anxiety: higher prevalence of late chronotype (OR = 2.6) and DSPS (OR = 2.4). For every SD increase of inattentive symptoms or ADHD symptoms index, OR for DSPS and extreme evening chronotype increased by 1.3.	N/A	N/A	No differences in BMI between groups.	ADHD symptoms, specifically inattentive symptoms, are associated with extreme evening chronotype in the presence of lifetime depression and anxiety.
N/A	ADHD vs controls: greater eveningness. Eveningness was associated with greater ADHD symptoms.	N/A	N/A	Eveningness is associated with more symptoms of ADHD.
Circadian rhythms: MPH treatment reduced urinary 6-OH MS excretion and lowered morning melatonin in ADHD patients.	ADHD symptoms improve after MPH treatment.	CDI improves after MPH treatment. Serotonin was lower in ADHD patients in the morning compared with controls; serotonin was not affected by MPH.	N/A	Stimulant treatment of ADHD reduces melatonin levels, which may have an impact on DSPS or chronotype.

(*Continued*)

Table 1 (*Continued*)

Author and year	Sample	Study design	Diagnoses	Measures
Table 1.4 Insomnia				
Vélez-Galarraga et al (2016)[99]	126 children with ADHD, 1,036 controls Sex: 504 males, 658 females Age (mean ± SD), years: ADHD: 11.25±3.25; controls: 10.83±3.75	Case–control	ADHD: K-SADS-PL, DSM-IV criteria Insomnia: PSG	Sleep: PSG Attention: ADHD-RS, CPT
Yoon et al (2013)[101]	126 adults with ADHD Sex: 93 males, 33 females Age (mean ± SD), years: 38.1±10.4	Cross-sectional	ADHD: CAARS-S:L, ASRS, SCID-I, TCI Insomnia: PSQI	Sleep: PSQI Sleepiness: ESS, FSS Attention: CAARS-S:L, ASRS
Moreau et al (2014)[97]	41 children with ADHD, 41 controls Sex: 24 males, 17 females Age (mean ± SD), years: ADHD: 9.74±1.69; controls: 9.57±1.62	Case–control	ADHD: CPRS-R, CTRS-R, K-SADS-PL Insomnia: ISI-C	Sleep: Actigraphy, CSHQ, ISI-C Attention: CPRS, CTRS, CBCL Socioemotional: CBCL
Corkum et al (2016)[98]	22 children with ADHD and 39 typically developing with behavioral insomnia Sex: 28 males, 33 females Age (mean ± SD), years: 9.11±1.96	Randomized controlled trial Intervention: "Better Nights/Better Days" distance sleep intervention or waitlist control	ADHD: K-SADS-PL Insomnia: DSM-IV criteria	Sleep: CHSQ Actigraphy Sleep evaluation questionnaire Attention: CBCL Socioemotional: CBCL
Brevik et al (2017)[47]	268 adults with ADHD, 202 controls Sex: 184 males, 286 females Age (mean ± SD), years: ADHD: 38.1±11.4; controls: 36.5±8.0	Case–control	ADHD: ASRS Insomnia: BIS	Sleep: BIS Attention: ASRS

Sleep differences	Daytime impairments			Conclusions
	Cognitive	Emotional	Physical	
ADHD vs controls: greater bedtime resistance, difficulty falling asleep, and sleep onset latencies longer than 30 minutes than controls. No differences in insomnia prevalence.	In children with ADHD: ADHD-RS ≥24 vs ADHD <24: higher prevalence of insomnia. Higher omission errors on the CPT were associated with shorter sleep duration.	N/A	N/A	In children with ADHD, more symptoms of ADHD were associated with a higher prevalence of insomnia, and more inattentive errors on the CPT were associated with shorter sleep duration.
Initial insomnia was the most common subjective complaint in adults with ADHD. ADHD-I vs ADHD-C: no differences in proportion of insomnia or sleepiness; greater PSQI scores and fatigue.	N/A	N/A	N/A	ADHD-I was associated with greater daytime fatigue and greater sleep disturbance.
Children with ADHD vs controls: increased sleep onset latency and night awakenings, higher insomnia severity, shorter actigraphic sleep time, longer sleep onset latency, lower sleep efficiency, and greater variability of sleep onset latency. Having a comorbid psychiatric disorder (in addition to ADHD) worsened these measures. Stimulant medication use was not associated with any differences in sleep.	N/A	N/A	N/A	Presence of ADHD is associated with increased sleep problems and insomnia severity.
Sleep intervention improved objective and subjective sleep onset latency, subjective sleep duration, bedtime resistance, and total sleep disturbance (vs no changes in waitlist control). This improvement was maintained at 6-month follow-up.	Sleep intervention improved CBCL scores, which includes attention problems. Improvement increased at 6-month follow-up.	Sleep intervention improved CBCL internalizing and externalizing scores. This improvement increased at 6-month follow-up.	N/A	Better nights/better days was effective in improving sleep and daytime functioning in children with insomnia that are either typically developing or with ADHD.
ADHD vs controls: 67% vs 29% insomnia prevalence. ADHD-C vs ADHD-I: higher prevalence of insomnia. Stimulant treatment vs no treatment: lower insomnia severity.	Insomnia severity was strongly correlated with inattentive symptom severity.	N/A	N/A	Insomnia is more prevalent in adults with ADHD, specifically in ADHD-C. Inattentive symptoms are correlated with insomnia severity.

Table 1 (*Continued*)

Author and year	Sample	Study design	Diagnoses	Measures
Table 1.5 Narcolepsy				
Ito et al (2018)[57]	77 adolescent and adult outpatients with narcolepsy type 2 or hypersomnia. Sex: 48 males, 29 females Age (M±SD), years: narcolepsy type 2: 25.7±5.8; narcolepsy type 2 + ADHD: 23.0±7.0	Cross-sectional	ADHD: DSM-IV criteria Narcolepsy type 2: self-reported symptoms and MSLT	Sleep: PSG Sleepiness: MSLT
Lecendreux et al (2015)[106]	188 children with narcolepsy. 67 healthy controls. Sex: 85 males, 90 females Age (median [range]), years: narcolepsy type 1: 14.0 (6.6–17.8); narcolepsy type 2: 10.3 (5.9–17.4); controls: 14.8 (7.0–17.9)	Case–control	ADHD: ADHD-RS Narcolepsy: ICSD-2 criteria, PSG, MSLT, CSF hypocretin-1 levels	Sleep: ISI Sleepiness: PDSS Attention: ADHD-RS Socioemotional: CDI
Filardi et al (2017)[108]	21 adults with narcolepsy type 1, 15 adults with narcolepsy type 2, and 22 healthy controls Sex: 26 males, 32 females Age (M±SD), years: narcolepsy type 1: 36±12; narcolepsy type 2: 36±13; controls: 35±12	Cross-sectional	ADHD: ASRS Narcolepsy: ICSD-3 criteria	Sleep: narcolepsy: PSG; controls: actigraphy. Sleepiness: ESS MSLT Attention ASRS; ANT Socioemotional: BDI; STAI; OCIr Physical: BMI.
Rocca et al (2016)[104]	29 children with narcolepsy type 1, 39 controls. Sex: 36 males, 32 females Age (M±SD), years: narcolepsy type 1: 11.52±2.89; control: 11.21±3.44	Case–control	ADHD: CBCL Narcolepsy: previous diagnosis by psychiatrist (criteria not specified)	Sleep: PSG Attention: CBCL Quality of life: PedsQL
Zamarian et al (2015)[107]	51 narcolepsy. 35 healthy controls. Sex: 46 males, 40 females Age (M±SD), years: narcolepsy type: 38.94±14.15. Control: 39.86±13.96	Cross-sectional	ADHD: None Narcolepsy: ICSD-2	Sleepiness: SSS Attention: Questionnaire on perceived deficits of attention, digit span, backward digit span, D2 attention test, RWT, IED, SOC, go/no go, auditory verbal learning test Socioemotional: HADS

Sleep differences	Daytime impairments			Conclusions
	Cognitive	Emotional	Physical	
Sleep: shorter stage N1, longer stage N3 in narcolepsy + ADHD compared with those with only narcolepsy. Sleepiness: narcolepsy + ADHD shorter REM sleep latencies on MSLT than those with only narcolepsy.	N/A	N/A	N/A	Narcolepsy type 2 + ADHD vs narcolepsy: greater daytime sleepiness.
In children with narcolepsy, ADHD symptoms were associated with longer sleep onset latencies.	Narcolepsy vs controls: more ADHD symptoms. Insomnia and fatigue were associated with increased inattention.	Narcolepsy + ADHD vs narcolepsy: significantly more depressive symptoms and lower quality of life.	N/A	Narcolepsy vs controls: more symptoms of ADHD. More ADHD symptoms are associated with more depressive symptoms.
In narcolepsy type 1, impaired attention was associated with greater sleepiness.	Narcolepsy vs controls: more inattentive and slower reaction times. Narcolepsy type 1 vs narcolepsy type 2 and controls: more hyperactive and worse alerting scores.	In narcolepsy type 1, higher ADHD symptoms were associated with higher depression scores.	Narcolepsy type 1 vs narcolepsy type 2 and controls: higher BMI	Narcolepsy vs controls: greater ADHD symptoms. ADHD symptoms in narcolepsy were associated with more depressive symptoms.
Total sleep time of 489±72 minutes in the narcolepsy group. Total sleep time was not reported in the control group.	Narcolepsy type 1 was associated with higher attention problems and ADHD scores. Treatment with sodium oxybate, but not with modafinil, was associated with improved attention and ADHD scores.	In participants with narcolepsy type 1, ADHD symptoms were associated with worse school functioning and higher psychosocial health.	In the narcolepsy type 1 group, there were no significant associations between ADHD symptoms and physical health.	Narcolepsy vs controls: more ADHD symptoms. ADHD symptoms in narcolepsy are associated with worse school and psychosocial health. Sodium oxybate treatment of narcolepsy is associated with reduced daytime impairment.
Sleepiness increased with testing in the narcolepsy group but not in the control group.	Narcolepsy vs control: greater subjective deficits of attention, worse selective attention, reduced verbal fluency, and fewer participants reached the go ceiling in the go/no go task. Subjective deficit of attention was associated with sleepiness and depression.	Narcolepsy vs control: greater depression.	N/A	Narcolepsy was associated with worse deficits of attention.

(*Continued*)

Table 1 (*Continued*)

Author and year	Sample	Study design	Diagnoses	Measures
Table 1.6 Various sleep disorders				
Miano et al (2016)[81]	15 children with ADHD Sex: 13 males, 2 females Age (mean ± SD), years: 10.6±2.2	Cross-sectional	ADHD: K-SADS-PL ADHD-RS Narcolepsy: ICSD-3 MSLT PLMD: PSG	Sleep: actigraphy CSHQ Video PSG Sleepiness: MSLT PDSS
Vogel et al (2017)[79]	942 adults Sex: 256 males, 686 females Age (mean ± SD), years: 48.5±14.2	Cross-sectional	ADHD: ASRS Sleep disorders: DSISD	Sleep: DSISD, SNS, ISI, Berlin questionnaire for OSA Chronotype: MCTQ Attention: ASRS
Hysing et al (2016)[94]	9846 adolescents Sex: 4,594 males, 5,252 females Age (mean), years: 17. SD not reported	Cross-sectional	ADHD: ASRS DSPS: ICSD-R Insomnia:Lichstein's criteria (2003)	Sleep: self-report ADHD: ASRS Socioemotional: SMFQ
Grünwald and Schlarb (2017)[100]	72 children with ADHD or subthreshold ADHD Sex: 57 males, 15 females Age (mean ± SD), years: 8.61±1.65	Cross-sectional	ADHD: DSM-5 criteria Sleep: CSHQ Socioemotional: KINDL Physical: KINDL	Sleep: CSHQ Attention: FBB-HKS
Bjorvatn et al (2017)[77]	268 adults with ADHD, 202 controls Sex: 183 males, 287 females Age (mean), years: ADHD: 38.1; controls: 36.5. SD not reported.	Cross-sectional	ADHD: DSM-IV criteria Sleep: GSAQ	Sleep: GSAQ

Sleep differences	Daytime impairments			Conclusions
	Cognitive	Emotional	Physical	
26.6% of children with ADHD had suspected narcolepsy 40% of children with ADHD had PLMD	N/A	N/A	N/A	Children with ADHD may have a high prevalence of narcolepsy and PLMD.
CRSD: the OR reporting an extreme evening type was 1.27 and 1.42 for overall ADHD and inattentive symptoms, respectively, for each increase in ADHD symptom severity. Insomnia: odds of having insomnia were significantly higher if ADHD was present. The OR of presenting insomnia was 1.67 if there were hyperactivity symptoms with an OR of 1.67. Severe symptoms vs none or mild: OR of 1.54, 2.42, and 1.55 for initial, middle, and terminal insomnia, respectively.	ADHD symptom severity classified as none, medium, and severe. Narcolepsy: ADHD symptom severity was not associated with narcolepsy. PLMD: PLMD was associated with severe overall ADHD and hyperactive symptoms. OSA vs non-OSA: OR of 1.22 for ADHD symptoms overall, 1.17 for inattention symptoms, 1.39 for hyperactivity symptoms, and 1.50 for severe overall ADHD symptoms.	N/A	N/A	ADHD symptoms are associated with PLMD, extreme evening chronotype, and insomnia. Inattentive symptoms were associated with OSA and extreme evening chronotype. Hyperactivity symptoms were associated with PLMD and insomnia.
Severe ADHD symptoms vs mild ADHD symptoms: 7.6% vs 2.8% prevalence of DSPS. 33.0% vs 11.4% prevalence of insomnia. They also had later bed times, wake up times, shorter sleep duration, and lower sleep efficiency on both weekdays and weekends.	Shorter sleep was associated with worse ASRS scores. This effect was stronger for inattentive symptoms than hyperactive symptoms.	N/A	N/A	ADHD symptoms are associated with greater prevalence of DSPS and insomnia. More symptoms are associated with shorter sleep, especially with inattentive symptoms.
ADHD-H vs ADHD-I: greater insomnia severity	SDB: higher SDB symptoms are associated with higher total ADHD symptoms. This association is stronger for hyperactivity, followed by impulsivity. SDB and inattentive symptoms were not correlated.	ADHD vs normative data: worse psychological well-being, self-esteem, friends and family quality of life, and daily/school functioning.	ADHD vs normative data: worse physical well-being	ADHD was associated with more SDB symptoms. Hyperactive symptoms were more strongly associated with SDB and insomnia than inattentive symptoms. ADHD was associated with worse socioemotional and physical well-being.
ADHD vs controls: more likely to report any sleep problems, loud snoring, breathing pauses during sleep, cataplexy, short sleep duration, daytime sleepiness, use of hypnotics, extreme evening types, restless legs, or periodic limb movements. Treated ADHD vs untreated ADHD: less likely to report sleep problems, cataplexy, and restless legs. ADHD-C and ADHD-H vs ADHD-I: more likely to report restless legs.	N/A	N/A	N/A	ADHD is associated with greater reporting of symptoms of narcolepsy, CRSD, RLS/PLMD, OSA/SDB, and insomnia. Treatment of ADHD is associated with better sleep and less symptoms of narcolepsy and RLS. Hyperactive symptoms of ADHD are associated with RLS.

(Continued)

Table 1 (*Continued*)

Author and year	Sample	Study design	Diagnoses	Measures
van der Heijden et al (2018)[93]	358 children Sex: 212 males, 146 females Age (mean ± SD), years: 9.02±2.06	Cross-sectional	ADHD: DSM-IV criteria Sleep: none	Sleep: CSHS, SDSC Chronotype: CCTQ

Abbreviations: 6-OH MS, 6-hydroxymelatoninsulfate; ABAS-II, Adaptive Behavior Assessment System, second edition; ADHD, attention-deficit/hyperactivity disorder; ADHD-C, ADHD combined subtype; ADHD-DC, ADHD Diagnostic Checklist; ADHD-I, ADHD inattentive subtype; ADHD-RS, ADHD Rating Scale; AHI, Apnea-Hypoapnea Index; ANT, Attention Network Task; ASD, autism spectrum disorder; ASRS, ADHD Self-Report Scale; AT, adenotonsillectomy; BASC-2: Behavior Assessment for Children, second children; BDI, Beck Depression Inventory; BIS, behavioral inhibition system; BMI, body mass index; CAARS, Conners' Adult ADHD Rating; CAARS-S:L, Conners' Adult ADHD Rating Scales – Self-report, Long version; CBCL, Child Behavior Checklist; CBT, core body temperature; CCTQ, Children's Chronotype Questionnaire; CDI, Children's Depression Inventory; CGI-P, Conner's Global Index, parent version; CHSQ, Children's Sleep Habits Questionnaire; CIDI, Composite International Diagnostic Interview; CPRS, Conner's Parent Rating Scale; CPRS-R, Conner's Parent Rating Scale, revised; CPT, Continuous Performance Test; CRSD, circadian rhythm sleep disorder; CSF, cerebrospinal fluid; CSHQ, Children Sleep Habits Questionnaire; CSHS, Children Sleep Hygiene Scale; CTRS, Conner's Teacher Rating Scale; DAS, Differential Ability Scale; DISC-IV, Diagnostic Interview Schedule for Children; DIVA 2.0, Diagnostic Interview for ADHD in Adults; DLMO, dim light melatonin onset; DSISD, Duke Diagnostic Interview for Sleep Disorders; DSM-IV, Diagnostic and Statistical Manual, fourth edition; DSM-IV-TR, Diagnostic and Statistical Manual, fourth edition, text revision; DSPS, delayed sleep phase syndrome; EDAH, evaluation of deficit of attention and hyperactivity; ESS, Epworth Sleepiness Scale; FBB-HKS, Symptom Checklist for Attention Deficit Hyperactivity Disorders; FSS, Fatigue Severity Scale; GSAQ, Global Sleep Assessment Questionnaire; HADS, Hospital Anxiety and Depression Scale; ICD-9, International Classification of Diseases, ninth revision; ICSD-2, International Classification of Sleep Disorders, second edition; ICSD-3, International Classification of Sleep Disorders, third edition; IED, intra-/extradimensional set shift; IRLSSG, International Restless Leg Syndrome Study Group; IQ, intelligence quotient; ISI: Insomnia Severity Scale; ISI-C, Insomnia Severity Index for Children; IVA-CPT, Integrated Visual and Auditory Continuous Performance Test; JSS, Jenkins Sleep Scale; KINDL, Questionnaire for Measuring Health-related Quality of Life in Children and Adolescents; K-SADS, Kiddie Schedule for Affective Disorders and Schizophrenia; K-SADS-PL, Kiddie Schedule for Affective Disorders and Schizophrenia, present and lifetime version; K-WISC-III, Korean Wechsler Intelligence Scale for Children, third edition; MCTQ, Munich Chronotype Questionnaire; MEQ, Morningness-Eveningness Questionnaire; MFFT-KC, Matching Familiar Figure Test for Korean Children; MOCI, Maudsley Obsessive Compulsive Index; MPH, methylphenidate; MSLT, multiple sleep latency test; MWT-B, multiple choice vocabulary test; NEPSY, A Developmental Neuropsychological Assessment; OCD, obsessive-compulsive disorder; OCIr, Obsessive-Compulsive Index-revised; OSA, obstructive sleep apnea; OSA-18, Obstructive Sleep Apnea-18; OSAHS, obstructive sleep apnea hypopnea syndrome; PDSS, Pediatric Daytime Sleepiness Scale; PedsQL, Pediatric Quality of Life Inventory; PLMD, periodic limb movement disorder; PLMI, periodic limb movement index; PLMS, periodic limb movement syndrome; PSG, polysomnography; PSQI, Pittsburgh Sleep Quality Index; REM, rapid eye movement; RLDI, Restless Leg Diagnosis Index; RLS, Restless Leg Syndrome; RME, rapid maxillary expansion; RWT, Regensburger Wortflussigkeits-Test; SCARED, screen for child anxiety related disorders; SCID-I, Structured Clinical Interview for DSM-IV Axis I Disorders; SDB, sleep-disordered breathing; SDQ, Strengths and Difficulties Questionnaire; SDSC, Sleep Disturbance Scale for Children; SF-36, Short form (36) Health Survey; SHQ, Sleep Health Questionnaire; SMFQ, Moods and Feelings Questionnaire; SNS, Swiss Narcolepsy Scale; SOC, Stockings of Cambridge; SRBD, Sleep Related Breathing Disorders questionnaire; SSS, Stanford Sleepiness Scale; STAI, State-Trait Anxiety Index; TCI, Temperament and Character Inventory; WISC-R, Wechsler Intelligence Scale for Children, revised; WURS-K, Wender-Utah Rating Scale, short form.

of apnea and hypopnea events per hour of sleep, in individuals with OSA with and without ADHD.[74]

Subjective measures

School-age children. N/A; Adolescents. N/A; Adults. Increased levels of self-reported loud snoring and breathing pauses during sleep in individuals with ADHD compared with healthy controls.[77]

Daytime impairments
Cognitive impairments
Subjective measures

Pre-school and school-age children. In children with SDB, significantly more symptoms of hyperactivity/inattention but not impulsivity were reported compared with healthy controls.[67,78] Adolescents. N/A; Adults. Individuals with OSA symptoms had high levels of self-reported inattention and hyperactivity when compared with individuals without OSA symptoms.[79]

Objective measures

School-age children. Performance of children who reported frequent snoring (over three times per week) was poorer on tasks measuring attention, executive functions, language, intellectual functioning, and information processing when compared with healthy children who did not snore as frequently[67] (less than two times per week). In addition, children with diagnosed OSA performed worse on measures of sustained attention compared with typically developing children.[72] Adolescents. N/A; Adults. N/A.

Emotional impairments

Pre-school and school-age children. Children with OSA and ADHD had lower ratings on quality of life compared with individuals with OSA alone.[80] Adolescents. N/A; Adults. Individuals with OSA and ADHD had lower ratings on quality of life and higher levels of reported symptoms of depression and anxiety than individuals with OSA alone.[74]

Sleep differences	Daytime impairments			Conclusions
	Cognitive	Emotional	Physical	
Insomnia: ADHD vs controls: shorter sleep duration and longer sleep onset latencies. DSPS: no differences in chronotype between ADHD, ASD, and healthy children. Eveningness predicted sleep problems in all three groups.	N/A	N/A	N/A	Children with ADHD have shorter sleep duration and longer sleep latency.

Physical impairments

Pre-school and school-age children. Severity of ADHD symptoms was associated with allergic rhinitis, adenoid hypertrophy, and tonsil hypertrophy in individuals with ADHD and OSA.[80] Adolescents. N/A; Adults. No difference was found in body mass index (BMI) between individuals with OSA and ADHD and OSA alone.[74]

ADHD and RLS

The present review includes seven studies (four cross-sectional, two case–control, and one randomized control trial) that examined the sleep characteristics associated with RLS and ADHD.

Sleep characteristics[81–85]
PSG

School-age children. A higher periodic limb movement disorder index was found for children with ADHD and RLS compared with healthy controls[83] and for children with ADHD alone compared with healthy controls.[82] Individuals with ADHD alone did not differ in periodicity of leg movements compared with healthy controls.[82] Children with ADHD and RLS showed prolonged sleep latency, increased number of stage shifts, awakenings, and increased percentage of sleep stage 1 compared with healthy controls;[83] Adolescents. N/A; Adults. Individuals with ADHD had a higher periodic limb movement disorder index, longer sleep latency, and increased periodicity of leg movements compared with healthy controls.[85]

Actigraphy

School-age children. Multiple night awakenings, sleep hyperkinesias, and periodic limb movements were found in children with ADHD.[62] Adolescents. N/A; Adults. N/A.

Subjective measures

School-age children. Children with ADHD reported more restless legs symptoms when compared with healthy controls.[84] Adolescents. N/A; Adults. Higher levels of ADHD symptoms were reported by individuals with RLS, but the association between RLS and ADHD was no longer significant when accounting for sleep disturbances.[86]

Physiological correlates

School-age children. No differences were found in serum transferrin and iron levels between children with ADHD and healthy controls.[84] Regarding ferritin levels two studies[84,87] reported no difference in ferritin levels between individuals with ADHD and healthy controls, whereas another study[81] reported overall low ferritin levels in individuals with ADHD. Adolescents. N/A; Adults. No differences were found in serum ferritin and iron levels between individuals with RLS with or without ADHD. In addition, iron and ferritin levels did not correlate with RLS severity scores.[87]

Cognitive impairments
Subjective measures
School-age children. N/A; Adolescents. N/A; Adults. N/A.

Objective measures

School-age children. Verbal IQ on the Wechsler Intelligence Scale was positively correlated with stages 3 and 4 of sleep and limb movement index with arousals. It was negatively correlated with stage 2 of sleep.[82] On the Matching Familiar Figure Test for Korean Children (MFFT-KC), an instrument designed to measure reflection-impulsivity, more response errors were associated with longer sleep time and limb movement index with arousals and longer reaction time was associated with shorter duration of stage 2 of sleep.[82] Adolescents. N/A; Adults N/A.

Emotional impairments

No studies were conducted to assess emotional outcomes in individuals with RLS and ADHD.

Physical impairments

School-age children. N/A; Adolescents. N/A; Adults. A study found that RLS participants were more likely to be obese (BMI >30) than participants without RLS (28.5% of the RLS group compared with 10.1% of healthy controls).[86]

ADHD and CRSD

The present review includes eight studies (two cross-sectional, four case–control studies, and two open-label) that examined the sleep characteristics associated with CRSD and ADHD.

Sleep characteristics
PSG

No PSG study was conducted in individuals with ADHD and CRSD.

Actigraphy

School-age children. N/A; Adolescents. N/A; Adults. An actigraphic study revealed that sleep start time was 2:20 hours later, and sleep duration 1:08 hours shorter, sleep midpoint was delayed by 1 hour and 52 minutes, and sleep efficiency was higher in adolescents with ADHD and DSPS compared with healthy controls.[69]

Objective circadian measures

School-age children and adolescents. Children and adolescents with ADHD (6–16 years) had higher urinary levels of 6-hydoxymelatoninsulfate (a urine melatonin metabolite) at daytime, nighttime, and over 24 hours compared with healthy controls.[88,89] Treatment with methylphenidate reduced urinary melatonin excretion and lowered morning melatonin in children with ADHD.[90] Adults. Dim light melatonin onset occurred 1 hour and 23 minutes later in individuals with ADHD and DSPS compared with healthy controls.[91]

Subjective sleep and circadian measures

School-age children. Inconsistent findings were found in children with ADHD manifesting greater eveningness in one of the two studies conducted to assess circadian tendencies in this population compared with healthy controls.[92,93] Evening chronotype was associated with more resistance to sleep, respiratory problems, and daytime sleepiness.[92] Adolescents. Individuals with higher ADHD symptoms (>90th percentile on the ADHD Self-Report Scale [ASRS]) reported later bed and wake up times, shorter sleep duration, and lower sleep efficiency compared with individuals with low ADHD scores (<90th percentile on ASRS).[94] Adults. Greater eveningness was found in individuals with ADHD compared with healthy controls. Eveningness was related to higher severity of the ADHD symptoms.[40,95]

Daytime impairments
Cognitive impairments
Subjective measures

School-age children. N/A; Adolescents. N/A; Adults. Delayed sleep timing and daytime sleepiness were associated with higher levels of reported inattention and hyperactivity in participants with ADHD and DSPD compared with healthy controls.[96] Evening chronotype was associated with higher levels of ADHD symptoms.[40,89,95]

Objective measures

No studies using objective cognitive measures were conducted in individuals with CRSD and ADHD.

Emotional impairments

No studies were conducted to assess emotional outcomes in individuals with CRSD and ADHD.

Physical impairments

School-age children. Psychosomatic symptoms (stomach aches, aches and pains, complains of headaches, seems tired) on the Conner's Parent Rating Scale were correlated to eveningness in the ADHD group.[92] Adolescents. N/A; Adults. N/A.

ADHD and insomnia

The present review includes nine studies (three cross-sectional, five case–control, and one randomized control trial) that examined the sleep characteristics associated with insomnia and ADHD.

Sleep characteristics
PSG

No PSG study was conducted in individuals with ADHD and insomnia.

Actigraphy

School-age children. Actigraphic studies[97,98] revealed longer sleep onset latency, lower sleep efficiency, and lower total sleep time in children with ADHD alone compared with

healthy controls. However, these measures were worse for children with ADHD and a comorbid psychiatric disorder (eg, anxious, depressed, oppositional symptoms) when compared with individuals with ADHD alone and healthy controls.[97] Adolescents. N/A; Adults. N/A.

Subjective sleep measures

School-age children. Parental reports described longer sleep onset delay,[97,99] shorter sleep duration, and more restless sleep in children with ADHD compared with healthy controls.[97] Children with ADHD hyperactive/impulsive subtype scored higher on measures of insomnia compared with individuals with an inattentive type,[100] and no differences in insomnia scores between children with ADHD and healthy controls were found in another study.[99] Adolescents. Sleep duration and time in bed were shorter for individuals scoring high (over 90th percentile) in self-reported ADHD symptoms compared with those with low scores (<90th percentile).[94] The association was stronger for individuals with ADHD-inattentive subtype compared with ADHD hyperactive or combined subtypes.[74] Adults. Subjective complaints of poor sleep quality, EDS sleep onset insomnia, and interrupted sleep as per the cutoff scores on the Epworth Sleepiness Scale and Pittsburgh Sleep Quality Index were prevalent in samples of individuals with ADHD compared with controls.[47] Sleep quality was poorer in individuals with ADHD and an inattentive subtype compared with individuals with a combined subtype.[101] Individuals with ADHD reported prolonged sleep latencies (>30 minutes) on the Pittsburgh Sleep Quality Index compared with controls.[102] Adult women with ADHD reported higher prevalence of insomnia (43.9% vs 12.2%) compared with women without ADHD.[103]

Daytime impairments
Cognitive impairments
Subjective measures
No studies using subjective cognitive measures were conducted in individuals with insomnia and ADHD.

Objective measures
School-age children. N/A. Adolescents. Individuals with ADHD and shorter duration of nighttime sleep had more omission errors compared with healthy controls on a measure of executive function.[99] Adults. N/A.

Emotional impairments
School-age children. Quality of life scores were reduced in children with insomnia and ADHD compared with healthy controls.[100] Adolescents. N/A. Adults. N/A.

Physical impairments
School-age children. N/A. Adolescents. N/A; Adults. N/A.

ADHD and narcolepsy
The present review includes six studies (four cross-sectional and two case–control) that examined the sleep characteristics associated with narcolepsy and ADHD.

Sleep and sleepiness
PSG
School-age children. PSG studies showed longer total sleep times, shorter sleep latency, and shorter onset of REM periods in children with ADHD and narcolepsy compared with healthy controls.[81,104] Adolescents and adults. Shorter stage 1 and longer stage 3 of sleep were found in adolescents and adults with narcolepsy and ADHD compared with individuals with narcolepsy without ADHD.[57]

Actigraphy
School-age children. Participants with ADHD and sleep problems, including three individuals with narcolepsy, displayed sleep efficiency of <90%.[81] Adolescents. N/A; Adults. N/A.

Multiple Sleep Latency Test (a diagnostic tool used to objectively measure sleepiness and early-onset REM sleep)[105]
School-age children. N/A; Adolescents and Adults. Individuals with ADHD and comorbid narcolepsy type 2 had shorter REM sleep latencies compared with individuals with narcolepsy type 2 alone.[57]

Subjective measures
Four studies used subjective measures to describe sleep outcomes (Children Sleep Habits Questionnaire, Pediatric Daytime Sleepiness Scale, Epworth Sleepiness Scale, Stanford Sleepiness Scale). For children, parents were the main respondents to the questionnaires. Clinicians also provided subjective information after interviewing the children.

School-age children. Higher levels of ADHD symptoms were associated with higher levels of reported sleepiness and fatigue.[81,106] Adolescents. N/A; Adults. Individuals with attention deficits and narcolepsy reported more sleepiness compared with healthy controls.[107]

Cognitive impairments
Subjective measures
School-age children. Higher levels of inattention was found in children with narcolepsy compared with healthy controls.[104,106] Poor sleep and fatigue in participants diagnosed

with narcolepsy were associated with increased levels of inattention;[106] Adolescents. N/A; Adults. Higher levels of inattention symptoms and higher hyperactivity scores were found in patients with narcolepsy compared with healthy controls.[108]

Objective measures

School-age children. N/A; Adolescents. N/A; Adults. When comparing individuals with ADHD and narcolepsy to healthy controls, no significant differences were found in attention span and verbal working memory.[107] However, reduced verbal fluency,[107] greater difficulty in performing under time pressure, poorer performance on measures of executive functions (Go/no go test,[107] Attention Network Test[108]) were observed in adults with narcolepsy and ADHD compared with healthy controls.

Emotional impairments

School-age children. Children with narcolepsy and comorbid ADHD symptoms had more depressive symptoms and decreased quality of life compared with healthy controls.[106] Adolescents. N/A; Adults. Higher depression and ADHD scores were found in individuals with narcolepsy type 1 compared with controls.[107,108]

Physical impairments

School-age children. One study found a higher proportion of overweight or obesity in children with narcolepsy compared with healthy controls.[106] Although the narcolepsy group did have a higher proportion of ADHD individuals and individuals with overweight and obesity, the association between ADHD and obesity was not examined. Adolescents. N/A; Adults. Higher BMI was found in individuals with ADHD and narcolepsy type 1 compared with participants with narcolepsy type 2 and healthy controls.[108]

Discussion

This review aimed to describe empirical studies pertaining to sleep abnormalities and outcomes in individuals with ADHD and comorbid primary sleep disorders in order to identify and address management challenges associated with treating these individuals.

Consistent with many previous studies, reviews, and meta-analyses, most of the PSG studies have failed in establishing consistent sleep differences in sleep architecture between individuals with sleep disorders with and without ADHD. However, a few differences have emerged. Children with ADHD and RLS were found to have an increased per-

centage of sleep stage 1 compared with healthy controls,[83] whereas for individuals with ADHD and narcolepsy, a shorter stage 1[57] and shorter REM latency[57,104] were found across all age groups compared with individuals without ADHD.

A few studies have also shown that children with ADHD and RLS and adults with ADHD alone have longer sleep latencies compared with healthy controls,[83,85] and children with ADHD and narcolepsy have shorter sleep latencies compared with healthy controls.[81,104] In addition, children with ADHD and narcolepsy were found to have lower sleep efficiency compared with healthy controls.[81] In an actigraphic study, only children with ADHD were found to have more night awakenings and increased level of hyperkinesias.[81]

Subjective sleep reports both from parents of children with ADHD and adults with ADHD have consistently reported high prevalence of sleep problems.[40,47,77,81,86,92,94,95,97,99,101,106,107] Higher level of reported sleepiness was found for individuals with ADHD and OSA[77] and individuals with ADHD symptoms and narcolepsy[81,106,107] compared with those without ADHD and healthy controls, respectively. Individuals with ADHD reported increased daytime sleepiness across studies[40,47,81,92,106,107] as well as shorter sleep duration[82,91,94,97] compared with healthy controls. Finally, having an evening circadian type was more prevalent for individuals with ADHD[40,89,92,95] compared with healthy controls.

Only a few empirical studies have examined daytime impairments in individuals with ADHD and comorbid primary sleep disorders. Regarding cognitive impairments, studies revealed higher levels of reported symptoms of hyperactivity and inattention in children with SDB[68,78] and narcolepsy[104,106] and adults with OSA,[79] DSPD,[96] and narcolepsy[108] compared with healthy controls. Studies using objective cognitive measures revealed variable impairments across disorders and age groups. Children with OSA symptoms had impairments in attention, executive functions, language, intellectual functioning, and information processing compared with those without OSA symptoms.[67,72] The impairment in executive functions and verbal fluency was also seen in adults with ADHD and narcolepsy[108] compared with healthy controls.[107] There were no empirical studies looking at cognitive impairments in individuals with ADHD and insomnia or RLS across the different age groups.

There is a dearth of empirical studies examining emotional impairments related to disrupted sleep in individuals with ADHD and primary sleep disorders. Lower perceived quality of life was reported in children with ADHD and SDB,[80] insomnia[100] and narcolepsy,[106] and adults with ADHD

and SDB[74] compared with healthy controls. Higher level of depression and anxiety symptoms were reported in adults with ADHD and OSA[74] and narcolepsy[107] alone compared with healthy controls. A complete lack of empirical data is noted for the assessment of emotional impairments in individuals with ADHD and RLS, CRDS, or adults with insomnia. Knowing that sleep disturbances significantly intensify emotional reactivity and negative mood and impair emotional regulation, this lack of information represents a significant gap in knowledge as well as a significant barrier to effective clinical management.

Scarce empirical data exist for physical impairments or comorbid conditions in individuals with ADHD and primary sleep disorders. For children with ADHD and SDB, an increase in medical comorbidities including allergic rhinitis, tonsillar, and adenoid hypertrophy was found compared with healthy controls;[80] however, this finding cannot be generalized across the age groups due to lack of empirical data. Furthermore, these medical comorbidities are unlikely to be present in adults since these structures (adenoids/tonsils) atrophy following puberty.[109] In addition to medical comorbidities, the presence of comorbid primary sleep disorders was associated with increased BMI. Adults with RLS[86] and narcolepsy[108] are both found to have higher BMI compared with individuals without RLS and healthy controls, respectively, and children with narcolepsy have increased overweight and obesity compared with healthy controls.[106] There are no empirical data regarding physical impairments or medical comorbidities for individuals with ADHD and insomnia across ages as well as children with ADHD and RLS and adults with ADHD and CRDS.

Clinical implications

The high prevalence of subjective complaints regarding sleep disturbances in individuals with ADHD across all age groups, and the prevalence of daytime symptoms of inattention and hyperactivity in individuals with primary sleep disorders, suggests that a baseline sleep evaluation during the initial assessment of ADHD as well as regular systematic screening for sleep problems is necessary component of ongoing ADHD management. This is of particular importance given that the presence of such sleep problems will likely decrease the efficacy of an intervention aimed solely at improving ADHD symptoms. As a first step, it is essential to delineate the nature of the reported sleep problems in order to eventually be able to properly treat them. It is also a possibility that there may be concomitant sleep disorders that are manifested simultaneously; therefore, having a

thorough and systematic approach that includes objective sleep measures such as PSG, actigraphy, Multiple Sleep Latency Test along with obtaining detailed clinical history of the sleep, and ADHD challenges will help in establishing a clear diagnosis.

In order to undergo such tests, the treating physician will need to have access to referral to a facility that is capable of performing them. In turn, a sleep specialist will need access to a physician able to diagnose ADHD as well as psychological comorbidities in order to have a clear baseline. Collaboration between health professionals will be essential in treating these individuals and will be an integral part of the initial assessment.

Furthermore, a particular challenge will surface when assessing an adolescent population. Developmentally, during adolescence, sleep needs will naturally change. A key differentiation between normal sleep changes (eg, regular delayed sleep) and a sleep disorder (eg, DSPS) will need to be properly established.

Following a delineation of each problem, establishing a clear timeline of symptoms will be helpful to evaluate whether the symptoms of ADHD or the sleep disorder have a temporal relationship or whether they are comorbid. Moreover, it will be essential to establish whether the sleep problem is a cause or a consequence of the psychiatric comorbidity or vice versa and whether this stands true for the individual across their life span. Knowing that there is a significant prevalence of sleep disorders in ADHD and vice versa may lead to misattributions of symptoms of inattention and hyperactivity, for example, to ADHD and not a consequence of a sleep disorder. This issue will also impact the psychosocial treatment strategy as well as the pharmacologic treatment by a sleep specialist or a psychiatrist.

In addition to establishing a clear diagnosis, determining its impact or associations with daytime neuropsychological, emotional, or physical impairments would allow to map the sequence and magnitude of the required interventions. For example, if sleep disruption contributes to daytime inattention or executive dysfunction, treating it might be an ideal first step prior to or in addition to prescribing stimulant medications to address these challenges. Similarly, if sleep disturbances play a role in emotional dysregulation or low mood, treating sleep disturbance should be an important step in addressing the sleep and the comorbid disorders. In these cases, having a multidisciplinary approach will allow for simultaneous evaluation and treatment and collaboration with the goal of improving both the primary problem and the associated symptoms (eg, daytime impairments).

In terms of treatment, the first step following assessment and diagnosis will consist of psychoeducation. Both the individual affected and the social entourage of these individuals (parents, spouses, etc) will need to have proper psychoeducation on ADHD symptoms as well as the particular sleep disorder in addition to its course, prognosis, treatment, and possible functional implications. Furthermore, education on normal sleep patterns and sleep hygiene will allow for nonpharmacological improvement of sleep.

Using medication to treat sleep disorders is widespread. Medication selection, particularly if treatment for ADHD is warranted, can be targeted to improve associated problems such as daytime impairments and should be integrated with behavioral strategies. For children with ADHD and SDB, surgical removal of the adenoids or tonsils is a first-line treatment,[110] whereas for adults with ADHD and OSA, the use of positive airway pressure devices, oral appliances, or surgery are recommended treatment options.[111] For individuals with ADHD and RLS, behavioral interventions could include modifying the sleep environment and treatment with iron supplementation[112] (eg, ferrous sulfate) or gabapentin[113] could be considered, in particular for a younger population. Treatment with dopaminergic agents such as pramipexole, ropinirole, L-DOPA, and a relatively new medication, rotigotine, in an adult population could also be an option.[114] For individuals with ADHD and DSPS, treatment with light therapy[115] and chronotherapy[116] can be explored as well as using timed melatonin treatment.[117] Treatment for individuals with ADHD and insomnia will vary according to age group, and in addition, a clear distinction between insomnia and DSPS will have to be made given that treatment for DSPS will be different than that for insomnia. For children with ADHD and insomnia, behavioral treatments such as positive reinforcement, scheduled awakenings, unmodified extinction, and faded bedtime could be starting options.[118] For adolescents with ADHD and insomnia, cognitive behavioral therapy for insomnia (CBT-I) can be an effective treatment.[119] In adults with insomnia, CBT-I, stimulus control therapy, relaxation training, sleep restriction, multicomponent therapy, paradoxical intention, and biofeedback can be used alone or in conjunction with sleep medication,[118] although treatment with pharmacotherapy for insomnia has weak evidence.[120] For individuals with ADHD and narcolepsy, treatment with modafinil, sodium oxybate, or psychostimulants is indicated and it can be supplemented with education on sleep hygiene.[121] Treating with psychostimulants would allow for the added benefit of treating both underlying disorders and not restrict the treating physician for the treatment of symptoms only.

Limitations and future directions

The limitations of available empirical evidence give rise to several challenges. A key challenge is integrating information from studies that differ in the participants included in the clinical and/or the control groups. Although all the studies included in the present work examined sleep and/or daytime impairments of individuals with ADHD and primary sleep disorders, some included only individuals with diagnosed ADHD in the study group, whereas others included individuals with sleep disorders only or individuals with a diagnosis of both ADHD and a primary sleep disorder. Studies also varied in the characteristics of the control group, with some comparing the study group with a different clinical group and others comparing the study group with healthy controls. In addition, some studies included individuals with psychological comorbidities or individuals undergoing pharmacotherapeutic treatment, making the sample more heterogeneous. The interstudy differences in the study and control groups limited the ability to generalize findings across studies in some cases that precluded direct comparison of studies. A second challenge in the present work was that, for children, many of studies used parent reports or clinician evaluations to obtain information on subjective sleep measures and daytime impairments. Due to the use of subjective and retrospective reports from parents, the results must be interpreted with caution. In adolescents, few studies assessed objective and subjective sleep impairments or daytime impairments, and overall there is a dearth of literature for this population. The present work was made even more challenging by the small number of longitudinal and experimental studies that have been published in this area. The lack of such studies limited the ability to establish a better understanding of the nature and the direction of the associations between primary sleep disorders and ADHD. An alarming shortage of empirical evidence on daytime impairments caused by sleep disturbances in individuals with ADHD was noted across all domains and all age groups. Furthermore, in the few studies to date that have examined daytime impairments, the cognitive, emotional, or physical outcomes were poorly defined and were inconsistent between studies. This significantly limited the ability of the review to ascertain the nature and magnitude of the impairments caused by the presence of a primary sleep disorder in individuals with ADHD, above and beyond or in combination with the impairments they present with as a result of their ADHD.

Future research should focus on the systematic and thorough evaluation of daytime impairments associated with the combined impacts of ADHD and sleep disturbances on indi-

viduals with both conditions. Such research should clearly define outcomes that take into consideration the manners in which cognitive, emotional, and physical impairment may manifest at different ages, and should apply those definitions systematically across disorders. Ideally, these studies would compare individuals with ADHD and each of the primary sleep disorders known to be associated with ADHD to individuals with ADHD alone and to healthy controls. Results of these studies are needed to better appreciate patient needs and to inform clinical management.

Additional studies should also be conducted to capture the clinical characteristics and daytime impairments of all age groups, in particular adolescents and elderly patients (for whom there is no available empirical evidence). In addition, longitudinal studies are needed that evaluate changes in sleep, ADHD, and potential impairment over time, and that track the impacts of interventions on the sleep and daytime functioning of individuals with ADHD and comorbid sleep disorders.

Disclosure

The authors report no conflicts of interest in this work.

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