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SCIENTIFIC INVESTIGATIONS

Restless sleep disorder in children with attention-deficit/hyperactivity disorder

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Study Objectives: Restless sleep is a very common parental complaint in children with attention-deficit/hyperactivity disorder (ADHD), but restless sleep has been seen in association with other comorbidities such as restless legs syndrome and obstructive sleep apnea. Restless sleep disorder (RSD) needs to be identified from other disorders when evaluating children with ADHD. In this study we aim to identify the prevalence of RSD in children with ADHD referred to our sleep center.

Methods: This is a retrospective study of children with ADHD who underwent polysomnography. The following diagnostic and descriptive data were obtained for each patient: age, sex, presence/absence of RSD, other sleep disorders, psychiatric comorbidities, and medications. RSD was diagnosed per diagnostic criteria.

Results: There were 66 children with ADHD. All of them underwent polysomnography, 17 were females, and 49 were males. Mean age was 11.6 years (\pm 3.6 standard deviation). The complaint of restless sleep was reported by the parents of 54 (81.1%) of the children; however, only 6 of them (9.1%) were diagnosed with RSD. Seventy-one percent had obstructive sleep apnea and 19.7% had restless legs syndrome. A significant number of patients had psychiatric comorbidities and were on various medications.

Conclusions: Although restless sleep is a common complaint reported in 81.1% of children with ADHD, only 9.1% had RSD. Most causes of restless sleep are secondary and associated with other sleep disorders, psychiatric comorbidities, or medication use.

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

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Restless sleep is a common parental complaint in pediatric sleep medicine particularly in children with attention-deficit/hyperactivity disorder. Restless sleep disorder has been identified as a new pediatric sleep disorder characterized by large body movements during sleep and daytime impairment.

Study Impact: It is very important to identify secondary causes of restless sleep from primary restless sleep disorder to establish the right treatment options for the child. In this study we identify the prevalence of restless sleep disorder among children with attention-deficit/hyperactivity disorder and identify other causes of restless sleep in children with attention-deficit/hyperactivity disorder.

INTRODUCTION

Restless sleep disorder (RSD) is a newly identified pediatric sleep disorder characterized by frequent nocturnal body movements involving large muscle groups, sleep disruption, and daytime impairment.¹ Parental concerns of frequent repositioning through the night have been noted from clinical interviews.¹ Video-polysomnography (PSG) analysis of the movements during sleep showed that children with RSD present with > 5 body movements per hour.² The following clinical findings have been included in the diagnostic criteria for RSD: concern for restless sleep, body movement index $> 5/h$, duration of the disorder for at least 3 months, movements occurring for ≥ 3 nights a week, sleep disturbance causing significant daytime symptoms, and the absence of specific medication effects or another explanatory medical or psychiatric disorder.

The recognition of primary (RSD) or secondary restless sleep is imperative in guiding the appropriate treatment options. The prevalence of RSD in a sleep medicine pediatric practice is

estimated to be 7.7%.³ RSD must be differentiated from restless sleep secondary to other sleep or medical disorders. In fact, the complaint of restless sleep is quite common in pediatric sleep medicine. Parent questionnaire-based studies inquiring if sleep was thought to be “restless” have shown a concern for restless sleep in 80% of children with sleep-disordered breathing (SDB),^{4,5} 80% of children with restless legs syndrome (RLS), and 89% of children with periodic limb movements during sleep (PLMS).⁶ Although RLS and PLMS have been studied in children with attention-deficit/hyperactivity disorder (ADHD), the prevalence of RSD in children with ADHD is unknown. Both ADHD and sleep-related movement disorders such as RLS and PLMS are thought to have dysregulations in central nervous system iron metabolism⁷ and dopaminergic neurotransmission.⁸ Iron is a cofactor for tyrosine hydroxylase, which is needed to convert tyrosine into levodopa, a precursor to dopamine. Furthermore, dopaminergic medication is used in the treatment of ADHD. These findings may point toward a common pathophysiological mechanism between ADHD and sleep-related

movement disorders. The aim of our study is to evaluate the prevalence of restless sleep and RSD in a pediatric sleep medicine-referred population with ADHD.

METHODS

Participants

A retrospective study of children with ADHD who underwent PSG at the Sleep Disorders Center of Seattle Children's Hospital in Seattle, WA, between April 2019 and March 2020 was carried out. Children with ADHD are referred to our sleep center. Sleep-related diagnoses were carried out according to the *International Classification of Sleep Disorders*, third edition.⁹ In addition, the recently published criteria for RSD were also applied to identify this condition among the sample of patients²: A) The child exhibits a pattern of sleep characterized by "restless sleep" or motor behaviors involving large muscle groups; these consist of frequent repositioning, moving bed sheets, or falling out of bed; B) The movements are exclusively sleep related, occurring at any time after sleep onset, and persist at intervals through the night; C) The movements occur almost every night and exceed 5/h of sleep; D) Sleep latency and sleep time are within expected for age; E) The nocturnal behaviors result in a significant complaint by the patient or parent as manifested by at least one of the following: i. Interference (or parental perception) with nocturnal sleep; ii. Impairment in daytime function (sleepiness or school performance); iii. Irritability or hyperactivity; F) The condition is not better explained by behavioral or medical disorders or medication effect. Criteria A to F must be met.²

The following diagnostic and descriptive data were obtained for each patient: age, sex, presence/absence of a sleep disorder such as RSD, RLS, periodic limb movements during sleep (PLMS) or periodic limb movement disorder, obstructive sleep apnea (OSA), insomnia, bruxism, presence/absence of epilepsy or a different neurologic disorder, psychiatric disorder (anxiety, depression, posttraumatic stress disorder), neurodevelopmental (autism) disorder.

The study was approved by the Institutional Review Board of the Seattle Children's Hospital.

Video polysomnography

PSG was performed according to the American Academy of Sleep Medicine criteria (AASM),¹⁰ and data were recorded using the Sandman Elite Natus system. Parameters recorded included electroencephalogram (2 frontal, 2 central, and 2 occipital channels that were referred to the contralateral mastoid), electro-oculogram, electromyogram of the submental muscle, electromyogram of the right and left tibialis anterior muscles, respiratory signals, effort signals for thorax and abdomen, oximetry, capnography, a single-lead electrocardiogram, and video and audio recording. Calibrations were performed per routine standard by technicians. Epochs were scored by a certified sleep technologist and a board-certified sleep physician according to the AASM criteria. OSA was defined as an obstructive AHI \geq 1 events/h.¹¹ Additional movement measurements were recorded by video observation by a board-certified sleep physician who

performed all the movement analysis in previous studies (L.D.R.).² The video PSG was reviewed epoch by epoch with the video on and the following were analyzed: large body movements that included arms, legs (not meeting criteria for PLMS), body position changes, both arm and leg movements without body repositioning, head movements without limb movements. All movements had to be clearly visible, and only movements lasting for at least 1 second were included. The number of movements were recorded as part of the diagnostic criteria for RSD; the total number of body movements divided by the hours of sleep was used to calculate the body movement index.

Statistical analysis

Between-group comparisons of PSG data were carried out by means of the Mann-Whitney *U* test. In consideration of the small sample size of the group with RSD, we also calculated the effect sizes, with the formula $r = z/\sqrt{N}$. With this approach, an absolute *r* value of .10 is considered to represent a small effect, $r = .30$ represents a medium effect, and $r = .50$ represents a large effect.¹²

RESULTS

In our study, we included 66 children with a historical diagnosis of ADHD evaluated consecutively in our sleep disorders center. All of them underwent a PSG, 17 were females, and 49 were males. Mean age was 11.6 years (\pm 3.6 SD). The complaint of restless sleep was reported by parents of 54 (81.1%) of the children; however only 6 of them (9.1%) were found to fit the criteria for RSD. Fifty children (75.8%) had comorbidities (full list reported in **Table 1**) including RSD and other sleep disorders, such as OSA, RLS, and PLMI $>$ 5/h, as well as psychiatric comorbidities such as anxiety and depression in various association. Approximately one-quarter of the children (18 = 27.3%) had multiple comorbidities. The remaining children with ADHD (16 = 24.2%) did not have any other comorbidity.

A large number of children were receiving medications for ADHD during the sleep study (**Table 1**). Forty (60.6%) children were medicated; 18 (27.3%) were on a single medication, most commonly a stimulant, and the rest of the children were on a combination of 2 or more medications. Twenty-six (39.4%) children were medication free at the moment of this study; out of the nonmedicated group, 3 children met the diagnostic criteria for RSD. Medications included stimulants (methylphenidate, amphetamines), guanfacine, antidepressants, clonidine (taken by 1 child), and prazosin (taken by 1 child).

Polysomnographic data are shown in **Table 2**. The low number of children who met the criteria for RSD does not allow for a sufficient statistical power for comparison. However, besides the obvious significant differences in respiratory (lower in the RSD subgroup) parameters and movement (higher in the RSD subgroup) parameters, children with ADHD and RSD displayed numerically higher values of sleep stage N2 and lower percentage of stage N3, percentage of REM sleep, and arousal index, with a low-to-moderate effect size.

Table 1—Comorbidities and medications in children with attention-deficit/hyperactivity disorder referred for sleep evaluation.

	Number	Percentage
Comorbidities		
Obstructive sleep apnea	47	71.2
Periodic limb movements during sleep > 5 events/h	17	25.8
Anxiety	17	25.8
Restless legs syndrome	13	19.7
Depression	10	15.2
Restless sleep disorder	6	9.1
Insomnia	5	7.6
Seizures	4	6.1
Bruxism	2	3.0
Asthma	2	3.0
Autism	2	3.0
Oppositional defiant disorder	2	3.0
Posttraumatic stress disorder	2	3.0
Tics	2	3.0
Nightmares	1	1.5
Snoring	1	1.5
Diabetes	1	1.5
Myelomeningocele	1	1.5
Medications		
Methylphenidate	17	25.8
Antidepressant	17	25.8
Amphetamines	11	16.7
Guanfacine	10	15.2
Antiepileptic	3	4.5
Antihistamine	1	1.5
Antihypertensive	1	1.5
Antipsychotic	1	1.5
Anxiolytic	1	1.5
Clonidine	1	1.5
Insulin	1	1.5

DISCUSSION

This preliminary observational study shows that although 81.1% of parents of children with ADHD complain that sleep is restless, only 9.1% of the children with ADHD fit the new RSD diagnostic criteria. This is very close to the 7.7% prevalence in the general sleep medicine referred population.³ A high percentage of our children with ADHD were found to have a comorbid sleep disorder such as OSA, RLS, or elevated PLMS. Coincidentally, restless sleep has previously been reported in 80% of children with these same disorders.¹³ OSA was found in 75% of our cohort in comparison to the literature, which shows the prevalence of OSA to be up to 57%.^{14,15} This difference

may be secondary to differences in cut-off criteria for the diagnosis of OSA (some studies have used higher apnea-hypopnea index) or may be due to a referral bias. Traditionally OSA is known to be a comorbidity that needs to be ruled out in the evaluation of ADHD, but other comorbidities may not be well known, which may result in more children with OSA symptoms being referred for PSG. Our results match previous studies on both RLS and increased PLMS.¹⁶ In fact, the prevalence of increased PLMS in ADHD has been reported in the range of 26–64%,^{16,17} which is very close to our finding of 25.8%. In terms of RLS, Oner et al¹⁸ found that 33.3% of children with ADHD met the criteria for RLS; this is a higher prevalence of RLS than in the general population. Other studies have found a lower prevalence of 6.8%.¹⁹ We also found a high prevalence of RLS in 19.7% of children with ADHD; this is within the range of findings in the literature. Furthermore, it has been documented that children with ADHD have low ferritin levels.²⁰ Iron supplementation may improve restless sleep in children with ADHD and has been shown to improve sleep in RSD.²¹

In our study, a high percentage of children with ADHD had a psychiatric comorbidity, in particular, anxiety (25.8%) and depression (15.2%). Our prevalence of psychiatric comorbidities is within the range found in previously published data. Joelson et al²² found 8.9% of patients with ADHD had anxiety and 13.6% had depression. Mitchison et al²³ reported anxiety in 41.9% of children and depression in 21.43%. Similar to sleep disorders, restless sleep has also been reported in patients with psychiatric comorbidities, with a prevalence that ranges from 31.7%²⁴ to 67.8%.²⁵ Restless sleep has also been reported in children with bipolar mood disturbance,²⁶ with anxiety disorder, and with conduct disorder.²⁷ ADHD medications have played a significant role in the treatment of daytime ADHD symptoms but may exacerbate sleep problems.²⁸

While various agents such as stimulants (methylphenidate and amphetamines), guanfacine, clonidine, and antidepressants are often used for ADHD and comorbid disorders in children, all of these medications affect sleep.²⁸ The majority of the patients in our study were on at least 1 medication at the time of their PSG study. The role of ADHD medications and their effect on sleep can vary depending not only on the class of the medication but also on the formulation (long acting vs short acting) and the time of day taken (to monitor for rebound symptoms after the effect of medications wears off). For example, Vigliano et al²⁹ found no significant change in sleep architecture after initiating immediate release methylphenidate. Boonstra et al³⁰ found that use of methylphenidate resulted in improved sleep consolidation and in generally better sleep. Based on these studies, methylphenidate does not seem to aggravate motor restlessness in sleep. Clonidine has been shown to help with improving sleep quality by reducing nighttime awakenings and sleep onset latency,³¹ but the effect on movements and restlessness is not known.

On the other hand, guanfacine, an alpha 2 agonist, has been shown to have negative effects on the quality of sleep reported as fatigue and tiredness in 20–40% of children,²⁸ adversely affecting daytime functioning.³² Rugino³³ reported a significant increase in wakefulness after sleep onset with guanfacine; however, its effects on movements during sleep have not been

Table 2—Polysomnographic findings in children with ADHD with and without RSD.

	RSD (n = 6)	No RSD (n = 60)	Mann-Whitney Test		Effect Size
	Median (IQR)	Median (IQR)	Z	P	r
Total sleep time, minutes	455.0 (417.5–479.5)	442.8 (389.5–495.8)	-.346	NS	-.043
Sleep latency, minutes	19.9 (12.9–41.2)	21.4 (11.9–50.2)	.535	NS	.066
Sleep efficiency, %	87.6 (78.1–91.0)	87.2 (76.2–91.8)	-.011	NS	-.001
Stage N1, %	9.4 (8.4–9.8)	7.9 (4.5–14.3)	-.424	NS	-.052
Stage N2, %	51.3 (42.1–62.5)	42.8 (37.8–50.1)	-1.717	NS	-.211
Stage N3, %	22.2 (16.8–28.7)	27.7 (21.8–32.4)	1.193	NS	.147
Stage R, %	15.6 (10.2–20.0)	19.5 (15.9–23.3)	1.528	NS	.188
Arousal index, events/h	9.5 (7.4–10.8)	11.3 (8.5–15.1)	1.338	NS	.165
Obstructive apnea-hypopnea index, events/h	0.9 (0.7–1.3)	2.8 (1.2–5.3)	2.844	< .0045	.350
Central apnea-hypopnea index, events/h	0.9 (0.3–2.5)	0.9 (0.4–1.5)	.000	NS	.000
Periodic limb movements during sleep index, events/h	0.8 (0.0–1.1)	1.1 (0.0–6.3)	1.026	NS	.126
Movements during sleep, events/h	6.0 (5.0–6.0)	2.0 (2.0–2.0)	-4.000	< .000063	-.492

ADHD = attention-deficit/hyperactivity disorder, IQR = interquartile range, RSD = restless sleep disorder. *Effect size $r = Z/\sqrt{N}$.

identified. In addition, 26% of patients in the study were found to be on antidepressants, which are well known to increase PLMS during sleep.³⁴

Although the effects of individual medications on sleep have been studied, there are insufficient data to predict the effects of combined medications on children's sleep; the compounding effect of polypharmacy is likely mediated by multiple variables, significantly limiting our ability to exactly delineate their effect on our study.

Also, we are not able to distinguish the impact of medications on the reported restlessness during sleep at present. With the exception of stimulants, which have a short half-life, a period of wash out of medications prior to a sleep study for evaluation of restless sleep may or may not be clinically possible. For instance, children with anxiety or depression who are stable on treatment may be at risk of worsening symptoms with discontinuation for a washout.

In conclusion, we have demonstrated that restless sleep is perceived to be a common parental concern in children with ADHD and it is most commonly associated with other sleep disorders, psychiatric comorbidities, or medication use. Only a fraction of these patients fit the criteria for RSD. This finding is very important in the pediatric sleep evaluation of children with ADHD, because it helps direct clinical evaluation, since by demonstrating that in children with ADHD and parental concern for restless sleep, restless sleep is most frequently secondary to other disorders rather than representing primary RSD. Also, an extensive literature review recently demonstrated that restless sleep is very often secondary to various sleep disorders.¹³ As our understanding of restless sleep in children expands, we can assess restless sleep in children with ADHD in a stepwise manner, searching for secondary causes of restless sleep and assessing if primary RSD is present once other comorbidities have been ruled out. Compared to the general sleep medicine-referred pediatric population, the prevalence of RSD does not

seem to be particularly high among patients with ADHD. Further evaluation of restless sleep in different clinical and community samples is needed to confirm this finding. The clinical practice guidelines for ADHD recommend the evaluation of other physical conditions that might coexist; although sleep apnea is listed as an example of one of these conditions, it is imperative for providers to be aware of other sleep disturbances such as RLS and periodic limb movement disorder that can contribute to restless sleep and daytime symptoms. Now with RSD as a primary sleep disorder, it is the authors' opinion that PSG should be part of the evaluation of every child considered to be diagnosed with ADHD, regardless of presence/absence of symptoms of OSA.

More research is needed to identify strategies to optimize sleep quality in children with ADHD, to evaluate RSD in ADHD subtypes, and to establish the prevalence of RSD in the general population.

ABBREVIATIONS

ADHD, attention-deficit/hyperactivity disorder
 OSA, obstructive sleep apnea
 PLMI, periodic limb movement index
 PLMS, periodic limbs movements of sleep
 PSG, polysomnography
 REM, rapid eye movement
 RLS, restless legs syndrome
 RSD, restless sleep disorder

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DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. The authors report no conflicts of interest.