

# New Research on the Complex Interaction of Sleep and ADHD

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Published online: 23 April 2015  
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**Abstract** Children with attention deficit hyperactivity disorder (ADHD) display higher rates of sleep problems such as bedtime resistance, sleep onset difficulties, night awakenings, difficulties with morning awakenings, sleep disordered breathing and daytime sleepiness. There has been a dramatic increase in new research of clinical significance to provide clinicians with the opportunity to better understand the association and possible causal relationships between sleep and ADHD. The objective of this paper is to provide an update on this literature over the past 3 years by examining any aspect of childhood ADHD and sleep and how it may inform clinical practice. As suggested by multiple lines of evidence, results from this review show that at the group level, there is a bidirectional impact of sleep and ADHD on each other and that both sleep and ADHD impairments may stem from common pathways. As hoped, effective intervention for either sleep or ADHD impacts both disorders thus opening the door to better treatment that goes beyond core symptoms to quality of life and functioning.

**Keywords** Attention deficit hyperactivity disorder (ADHD) · Sleep disordered breathing · Sleep onset difficulties · Neurobehavioural · Neurocognitive

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This article is part of the Topical Collection on *Sleep and Psychological Disorders*

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## Background

Sleep disturbances and disorders are one of the most common comorbidities or conditions associated with attention deficit hyperactivity disorder (ADHD) [1]. Reviews of sleep and ADHD to date have indicated that there appears to be an overlap between symptoms and features of ADHD and the neurobehavioural and neurocognitive effects of sleep disorders [2, 3].

The relationship between ADHD and sleep has been well documented in systematic reviews [2, 4, 5] and meta-analyses [6, 7]. Disturbed sleep can mimic ADHD in individuals referred for symptoms of ADHD [8]. Children with ADHD display higher rates of sleep problems such as bedtime resistance, sleep onset difficulties, night awakenings, difficulties with morning awakenings, sleep disordered breathing and daytime sleepiness than non-ADHD controls according to subjective ratings and sleep diaries completed by parents [6, 9]. On actigraphy, children with ADHD displayed increased sleep onset latency, less true sleep time on actigraphy monitoring, excessive daytime sleepiness as measured by a standard test compared to non-ADHD controls, and lower sleep efficiency on polysomnography [6]. Rates of sleep problems vary depending on demographics, the type of measurement (i.e. subjective vs. objective), and have been cited as being as high as 70 % of youth with ADHD [10].

There is a complex association between difficulties with sleep and ADHD, which is difficult to unravel due to overlapping symptoms and impairments, how and when children are evaluated, and a variety of methodological factors. ADHD may impact self-regulation and the developmental skills necessary to entrain circadian rhythms. Difficulties with sleep impact attention, inhibition, self-regulation and executive function in children with and without ADHD but have a greater cumulative impact on ADHD youth [11]. Both sleep

disorders and ADHD may be related by similar etiologies, specifically disruption in dopaminergic and melatonergic pathways. Increased understanding of these mechanisms will better inform the management of ADHD and sleep problems. Although it has long been observed that assessment of sleep requires an assessment for ADHD, more recently, it has been recommended that an assessment for ADHD requires evaluation of sleep [2].

There remains a number of concerns when evaluating the relationship between ADHD and sleep. Prevalence rates of specific sleep problems differ depending on several factors, including ADHD subtype, psychiatric comorbidities and medication use. For example, children with the inattentive subtype in one study displayed fewer night-time sleep problems than those with the combined subtype [12]. This requires further replication, and it is unclear if it is the subtype or severity of ADHD that is driving the relationship. In addition, despite being the first line of treatment for ADHD, methylphenidate and amphetamine stimulants have been shown to be associated with a greater number of sleep difficulties such as increased sleep onset latency and decreased duration of sleep [1], with decreased sleep time associated with increasing dose [13]. Melatonin has been shown to be effective in the reduction of sleep latency problems both for children not medicated [14] and medicated with stimulant medication [15].

Cortese et al. [16] conducted a review of the evidence between sleep and alertness in children with ADHD, controlling for potential confounding factors. They found 13 relevant studies, most of which looked at small samples. These authors concluded that children with ADHD had higher daytime sleepiness, more movements in sleep and higher apnea-hypopnea indices. They noted that epidemiological studies would be needed to assess the mechanisms underlying the association between sleep, alertness and ADHD in the general population using rigorous and standardized assessment criteria.

There are methodological issues that limit our ability to research the association of sleep and ADHD, or the attempt to assign causal inferences. At this point in time, there is robust research that clearly indicates a strong association of sleep problems with ADHD [1] in children and adolescents. As yet, there is only a paucity of studies examining sleep in adults with ADHD and there may be important developmental differences [17, 18]. Nonetheless, our understanding in children of some causal relationships has increased markedly over the past decade. We know that stimulants can cause insomnia and frequently exacerbate it when starting a medication trial or when the dose is increased [9]. Furthermore, we know that sleep deprivation causes or compounds difficulty with attention. We anticipate that both ADHD and sleep disorders may represent a final common pathway emerging out of common neurobiological deficits and environmental factors. For example, disruptions in dopamine and melatonin metabolism

would be expected to impact both sleep and ADHD. We also do not know if the dysregulation associated with ADHD ‘causes’ a developmental difficulty with entrainment of circadian rhythms. Night to night variability may exacerbate this, and variability in all settings is a hallmark of environments that predispose someone toward ADHD. We know that there are a minority of children who present with ADHD who may actually have a primary sleep disorder, but far more common are children who have both ADHD and sleep problems. We also know that certain sleep problems, such as obstructive sleep apnea, are associated with increased risk of ADHD, and successful treatment may reduce ADHD symptoms in a minority of individuals [19]. It has, for example, often been noted that the behavioural presentation of an ADHD child is not unlike the behaviour of an overtired child. There is suggestive evidence that ADHD is associated with distinct circadian rhythm patterns, such as the tendency to have a delayed sleep phase (i.e., being a night owl), but again, we do not understand the causal nature of this association [11, 20].

## Objectives

Since the last major review of ADHD and sleep [21], there has been considerable new research to provide clinicians with the opportunity to better understand the association and possible causal relationships between sleep and ADHD. The objective of this paper is to provide an update on this literature and how it may inform clinical practice.

We make the assumption that sleep and ADHD are interdependent in multiple ways but that a better understanding of the nature of this relationship may allow clinical intervention leading to improvement in both conditions. Sleep disorders and ADHD may lead to a vicious cycle in which insomnia leads to (or exacerbates) ADHD, and ADHD (and its treatment) further leads to worsening insomnia. If this was to be the case, then understanding of both conditions might lead to greater improvement than would be obtained with a focus on either condition alone.

## Methods

Recent and relevant publications were located using the keywords “ADHD” and “sleep” with PubMed, Google Scholar and PsycINFO. Selected articles included quantitative research published since 2012 that examined any aspect of childhood ADHD and sleep and excluded redundant case studies. Reviews were also excluded from the primary search. The selected articles and methodologies are displayed in Table 1.

**Table 1** Selected articles and methodologies

Authors	Year	Population	Topic	Findings
Scott, Blair, Emond, Fleming, Humphreys, Henderson & Gringras	2013	Avon longitudinal study (N=8195 total, N=173 with ADHD)	Epidemiological	Parent report at eight time points from birth to 11 years found children with ADHD to sleep less than peers. However, absolute difference was small and restricted to night-time sleep. Those with ADHD had more night wakings starting at age 5. Age-specific decreases in sleep of >1 SD predicted ADHD at 3–5 years
Moreau, Rouleau & Morin	2013	N=82 (50 % with ADHD)	Objective studies	Children with ADHD had more severe sleep disturbances according to parent report, and long sleep latency, lower sleep efficiency and lower total sleep time according to actigraphic recordings
Akinci, Oztura, Hiz, Akdogan, Karaarslan, Ozek, et al.,	2015	N=28 (8 girls)	Objective studies	Reduced total cyclic alternating pattern rate and duration of cyclic alternating pattern sequences were associated with a selective decrease of A1 index during stage 2 NREM sleep. SpO <sub>2</sub> in total sleep was also slightly decreased, even though they did not find a difference in sleep disordered breathing
Mohammadi et al.	2012	N=60, age 7–12	Melatonin	Administration of melatonin along with methylphenidate can partially improve symptoms of sleep disturbance
Molina-Caballo et al	2012	N=179, 136 with ADHD	Melatonin	ADHD patients showed reduced morning serotonin. Melatonin did not differ between ADHD and control. Melatonin was higher in children with ADHD-Hy. Methylphenidate was related to subtle changes in daily fluctuations and concentrations of serotonin and melatonin
Langberg, Dvorsky, Marshall, Evans	2013	N=100	Insomnia is associated with inattention and executive dysfunction	Self-reported daytime sleepiness significantly predicted parent-rated homework problems and academic impairment and teacher-related academic impairment above and beyond symptoms of ADHD. Did not predict grade point average or teacher-related academic impairment
Langberg, Dvorsky, Becker, Molitor	2014	N=62	Insomnia is associated with inattention and executive dysfunction	Self-reported daytime sleepiness predicted school maladjustment, overall functional impairment and the number of D and F grades above and beyond self and parent report symptoms of ADHD. However, it did not predict overall GPA
Moreau, Rouleau & Morin	2013	N=43 (58 % male)	Insomnia is associated with inattention and executive dysfunction	Parent reports of sleep disturbances were not associated with attention and EF problems. Low sleep efficiency as related to attention, lower total sleep time was associated with a wide range of EF problems even when other confounders were controlled
Hansen, Skirbekk, Oerbeck, Wentzel-Larsen & Kristensen	2014	N=137	Insomnia is associated with inattention and executive dysfunction	Found significant associations between parental reports of sleep problems and performance on attentional functioning for children with ADHD and anxiety.
Hiscock H, Sciberras E, Mensah F, Gerner B, Efron D, Khano S, Oberklaid F	2015	N=244 families	Psychosocial treatment	Found that the behavioural sleep intervention was associated with substantial and sustained benefits for both the children and their families. These results included improvement in the children's ADHD symptoms, sleep, health quality of life, daily functioning and teacher-reported behaviour. The author's concluded that a brief, behavioural intervention can lead to substantial benefits for both children and their families

## Results

### Epidemiological Associations of Sleep Disorders and ADHD

Current research has largely replicated the conclusions of earlier studies, providing robust evidence confirming the association between sleep and ADHD. Scott and colleagues [22] followed 8195 children from birth to 11 years with eight follow-up time points. In this study, they found children with ADHD slept less than their peers due to later bedtimes, although the absolute difference was small and restricted to nighttime sleep. They found that those children with ADHD had more night-waking starting at age 5. Interestingly, age-specific decreases in sleep duration measured by parent questionnaires of more than one standard deviation were predictive of an ADHD diagnosis. Likewise, in a sample of youth ( $N=137$ , age 7–13), Hansen and colleagues [23] also found significant associations between parental reports of sleep problems and performance on attention measures for children with ADHD and comorbid anxiety. We can therefore now say that there is clinical and epidemiological evidence indicating that children presenting with either ADHD or sleep problems will be at greater risk for the other disorder.

### Objective Studies

The first landmark review of the relationship between ADHD and sleep [24] noted a conundrum in which subjective parent reports frequently noted sleep disturbance as a complaint, while there was very little objective evidence of alterations in sleep architecture on polysomnograms. Later, authors hypothesized that this inconsistency might be explained by night to night variability in sleep which would not be detected in a polysomnogram done in one or, at most, two nights [25]. In addition, it may be that polysomnograms may be insensitive to naturalistic factors that trigger sleep impairment in the home environment but not in the lab setting, such as ambient noise, stress related to homework or a parent that is not sleeping. The most recent study of sleep architecture has now found evidence of abnormality in the microstructure of sleep that is not found in the macrostructure of sleep [26]. The authors found reduced total cyclic alternating pattern rate and duration of cyclic alternating pattern sequences were associated with a selective decrease of A1 index during stage 2 NREM sleep. SpO<sub>2</sub> in total sleep was also slightly decreased, even though they did not find a difference in sleep disordered breathing.

Early studies showed actigraphic changes in children with ADHD, demonstrating sleep onset insomnia (SOI), decreased sleep duration, sleep variability and sleep efficiency [20, 27, 28]. Actigraphy has, therefore, been a particularly useful tool, which provides somewhat more objective evidence than parent report while remaining naturalistic enough to be able to

capture the sleep impairments that occur in the homes of children with ADHD. In 2014, Moreau [29] replicated previous actigraphic studies comparing children with ADHD and controls on both parental and actigraphic measures of sleep. Parental reports, as expected, indicated more severe sleep disturbances. Actigraphy demonstrated longer sleep onset latency, lower sleep efficiency and lower total sleep time. Of note, in this study, there were no differences in sleep measured by actigraphy between children on a stable medication dose and untreated children. Of even more interest is that only the subgroup of children with comorbid psychiatric symptoms (i.e., learning disability, communication disorder, oppositional defiant disorder or generalized anxiety disorder) differed from the control group. The authors concluded that clinicians should systematically attend to sleep disturbances in children with ADHD, particularly when other psychiatric symptoms are also present as these children would be at even greater risk than children with ADHD alone.

### Melatonin

In healthy individuals, the melatonin rhythm is closely associated with the sleep cycle and this relationship has been shown to be disrupted in children with ADHD [30]. In individuals with ADHD and insomnia, there is a delay of nocturnal melatonin onset and differences in melatonin rhythm waveform [31]. This has led to research on possible alterations in melatonin or other neurotransmitters in children with ADHD and insomnia. The demonstration that exogenous melatonin can be used as a sleep aid for children with ADHD [32] further increased interest in understanding the basic biology of regulation of sleep and the pathophysiology of ADHD. Mohammadi and colleagues [33] replicated this finding, and their results were consistent with previous research. In a sample of 60 youths with ADHD between the ages of 7 and 12, melatonin along with methylphenidate led to improvement in symptoms of sleep disturbance. The replication of previous studies [14, 32] strengthened their findings. The designs of these three randomized trials looking at melatonin as a treatment for insomnia in children with ADHD are all quite different, but nonetheless come to the same conclusion. If melatonin is a fairly robust method of intervention for ADHD insomnia, we need a better explanation of the biological underpinnings of this relationship.

Molina-Carballo and colleagues [34] investigated the effect of chronic administration of prolonged release methylphenidate on daily variations in blood serotonin (5-HT), melatonin and on the excretion of the 6-sulphatoxy-melatonin (the primary metabolite of melatonin) in urine. In a sample of 179 children (mean age=9.70 years, SD=2.55), 136 of which met criteria for ADHD as per the DSM-IV, blood samples were drawn at 09:00 and 20:00, and urine was collected at 09:00 and 21:00. Participants with ADHD took prolonged release

methylphenidate and were reassessed after approximately 4 months. The 43 children who did not have ADHD had a higher 5-HT concentration in the morning as compared to ADHD patients. Baseline serum melatonin did not differ between children with ADHD and controls; however, when examined further, baseline serum melatonin was higher in children with ADHD hyperactive type. The use of methylphenidate was related to subtle changes in daily fluctuations in which melatonin was lower in the morning and slightly higher in the evening. However, the article failed to relate these results to a decrease in sleep onset delay. Further research would be needed to further delineate how stimulants impact melatonin and how melatonin impacts circadian levels of the neurotransmitters involved in ADHD.

### **Insomnia is Associated with Inattention and Executive Dysfunction**

Several recent studies focused on the effects of sleep on academic related outcomes. The first study found that in a sample of middle school children ( $N=100$ , mean age=11.91 years) self-reported daytime sleepiness significantly predicted parent-rated homework problems, and academic impairment as well as teacher-reported academic impairment. Importantly, these relationships were significant above and beyond the impact of ADHD symptoms on these outcomes [35]. Similar results were found for college age students. Self-reported daytime sleepiness predicted school maladjustment, overall functional impairment and the number of D and F grades above and beyond self and parent report symptoms of ADHD. However, it did not predict overall grade point average [36].

We know that executive function deficits are common in youth with ADHD, but not specific to the disorder. We also know that difficulties with organization are a major predictor of adult outcome in their own right [37]. Results from population-based studies also suggest a relationship between sleep disturbances and cognitive functioning [38]. In a sample of 43 children (mean age=10.1 years), Moreau [39] did not find that parental reports of sleep disturbances were associated with attention and executive functioning problems. However, they did find that objectively measured lower sleep efficiency was associated with increased variability in attention and that lower total sleep time was associated with a wide range of executive functioning problems as reported by parents. Likewise, Hansen and colleagues [23] found an association between parental reports of sleep problems and performance on attentional function in children with both ADHD and anxiety.

Most recently, an interesting study [40] further explored the relationship between sleep and attention by examining whether poor sleep was a risk factor for attention problems in both children with ADHD and typically developing children. The authors found that while sleep problems impacted alerting and

executive attention in all children, executive attention in children with ADHD may be particularly vulnerable to the negative effects of poor sleep. The authors note that these findings highlight the importance of ensuring all children and especially children with ADHD are getting good quality sleep to optimize attention.

### **Psychosocial Treatment**

The first evidence that sleep hygiene may be a possible treatment for abnormal circadian rhythms was found in the Weiss et al. [32] double-blind, placebo-controlled study of melatonin for sleep onset insomnia in children with ADHD on stimulants. The intervention for these children was gated such that only children who did not respond to sleep hygiene went on to be randomized to melatonin treatment. In this sample, sleep hygiene alone led to remission of SOI to less than 30 min in 42 % of the sample. The definition of a sleep hygiene responder was that they no longer met inclusion criteria of SOL > 60 min. The authors concluded that a combination of sleep hygiene and melatonin is likely to improve initial insomnia without the recourse of hypnotics.

Hiscock and colleagues [41] have published the first randomized, controlled trial of a brief sleep hygiene intervention in its own right. The intervention consisted of two face-to-face fortnightly (i.e., 2 weeks) consultations with a trained clinician. In the first consultation, the clinician i) assessed the child's sleep problems; ii) elicited parental goals for sleep; iii) provided information on sleep, sleep cycles and sleep hygiene; and iv) formulated a behavioural sleep management plan tailored to the child. Parents were asked to complete a sleep diary between the first and second visit. On the second visit and follow-up telephone call, the clinician reviewed the sleep diary, reinforced strategies, and helped to troubleshoot any problems. The authors found that the behavioural sleep intervention was associated with substantial and sustained benefits for both the children and their families. These results included improvement in the children's ADHD symptoms, sleep, health, quality of life, daily functioning and teacher-reported behaviour. The authors' concluded that a brief, behavioural intervention can lead to substantial benefits for both children and their families.

### **Discussion**

ADHD is a neurobehavioral disorder whose impact is not confined to the school day and, in fact, may represent a 24-h disorder associated with impaired nocturnal and diurnal arousal [42]. In recent research, the importance of night to night variability and effects on attention has been highlighted. The role of circadian rhythm sleep disorders causing or exacerbating ADHD have been demonstrated, linking hyperarousal in

the evening and attention impairment during the day. ADHD and sleep are not just comorbid, but the day and night manifestations of underlying physiological and neuropsychiatric deficits.

In 2012, Owens and colleagues [43] described several areas worthy of further research. The authors were working from a theoretical framework in which it was hypothesized that an enhanced understanding of the complex mechanisms regulating sleep promotion, wakefulness and attention might contribute new insights regarding the core impairments in either disorder. Among other things, they suggested we needed to better understand how alterations in circadian rhythm contribute to ADHD and explore evidence-based behavioural interventions for sleep disorders in ADHD patients.

The following year, the same authors provided a consensus statement on evidence-based clinical recommendations for intervention in sleep and ADHD stating that both behavioural techniques and melatonin were indicated as interventions for sleep problems in ADHD [21]. It was clear, even then, that we needed treatment strategies to optimize sleep in ADHD and to mitigate the added impact of the impairment caused by insomnia and excessive daytime sleepiness to the cognitive and behavioural impairments of ADHD. It was also clear that characteristic ADHD dysregulation was driving the deficits in entraining circadian rhythms in children with ADHD and thus contributing to eveningness. In the same year, Kooij [44] demonstrated that this was not only true for children but was also consistent at all stages of development.

Recent scientific advances help to clarify the conundrum identified by Corkum [24] as to why sleep was such an important complaint by patients, in the face of a failure to demonstrate objective differences in sleep between ADHD and controls, as polysomnographic studies failed to identify night-to-night variability, and *in natura* sleep impairment. Indeed, failure to show polysomnographic differences between ADHD and control subjects did not mean that patients were complaining of something that was not there but that early methods of ‘objective’ assessment of sleep were inadequate to capture the objective differences in sleep in ADHD patients.

In this paper, we have been able to describe new research that has successfully addressed many of the questions raised by the sleep working group 3 years ago [2, 45]. We have a new body of literature using epidemiological, objective, case control and randomized controlled intervention trials of melatonin and behaviour management—all refining our understanding of the relationship between ADHD and sleep. Epidemiologically, we have established age-specific differences in sleep duration measured by parent questionnaires of more than 1 standard deviation were *predictive* of ADHD diagnosis. Objectively, refined polysomnograms not only examined sleep architecture but also have been able to identify microstructural differences in sleep between ADHD and controls.

In 2013, we had level 1 evidence, more than two double-blind, placebo-controlled trials [14, 32], using different research methodologies in different populations to demonstrate that exogenous melatonin could be used as an intervention to regulate sleep in individuals with ADHD. We knew sleep hygiene alone could impact initial insomnia in children with ADHD and that melatonin could further augment that effect in those children who did not achieve remission with sleep hygiene alone [15]. Even more interesting, this relationship held up in the reverse direction. Van der Heijden and colleagues [14] showed that not only was it possible to alter sleep through behavioural interventions but that regulating sleep with melatonin led to improvements in sleep behaviour. We continue to replicate and further elaborate on the robust and bidirectional relationship between sleep hygiene and melatonin. Mohammadi and colleagues [33] replicated previous randomized control trials of melatonin for ADHD insomnia using yet another research design.

New evidence suggests that methylphenidate, a first-line intervention for ADHD, may also impact melatonin levels. Molina-Carballo and colleagues [46] found that administration of methylphenidate was related to subtle changes in the daily fluctuation of melatonin in which melatonin was lower in the morning and slightly higher in the evening in children with ADHD. This is a very interesting finding that needs further study, especially since these changes in fluctuations in melatonin did not translate into what would be an expected improvement in initial insomnia.

Multiple studies using different methodologies and emerging out of different areas have clearly established that insomnia and daytime sleepiness predict of cognitive, academic and executive function impairment [23, 36, 39]. This has led to public health interventions such as delaying the start of the school day as a way of mitigating sleep deprivation and optimizing learning [47, 48].

Most recently and long overdue is the first randomized controlled study of a manualized behavioural intervention specifically targeting sleep in children with ADHD [41]. This study established that the sleep intervention was associated with substantial and sustained benefits. The children receiving this intervention had improvement in ADHD symptoms, although the target of intervention was sleep. They also showed improved behaviour, health-related quality of life and daily functioning, all of which go well beyond the core symptoms targeted by previous interventions for ADHD. In addition, the parents also showed improvement with fewer days late for work.

This brings us back full circle to where we started. Parents had always told us that their ADHD children were struggling with sleep and overtired. Children with ADHD had long been observed to resist going to bed, complaining that they ‘could not turn their thoughts off’. Since the clinical and research community began to appreciate that these patient complaints

were both a real and serious source of impairment, it has become possible to develop effective and evidence-based interventions that target both sleep and ADHD. In 2012, we were aware that diagnostic assessment had to address both sleep and ADHD and that intervention for both disorders was necessary to optimize the outcome of either one. The last 3 years have allowed us to refine exactly why this is true and how to intervene. Future research directions will be able to exploit new technologies and methods to allow us to marry objective measurements with naturalistic settings using home-based polysomnography. Mobile technology (e.g. tablet and cell phone)-based methods of actigraphy have made it possible to obtain objective methods of monitoring sleep at home, not only collecting large amounts of data but also allowing us to use actigraphy as part of intervention. Future studies of sleep and ADHD will bring together the best of these epidemiological, objective, subjective and physiological methods.

## Conclusion

Five years ago, the idea that there was a complex association between ADHD and sleep was a hypothesis. As suggested by multiple lines of evidence, it is clear that at the group level, there is a bidirectional impact of sleep and ADHD on each other and that both sleep and ADHD impairments may stem from common pathways. As hoped, effective intervention for either sleep or ADHD impacts both disorders thus opening the door to better treatment that goes beyond core symptoms to quality of life and functioning. It is still an open question whether treatment of both day (ADHD) and night (sleep) abnormalities in alertness leads to a more than additive improvement. New research on the complex associations between sleep and ADHD has and will continue to lead to better clinical interventions and improved patient outcomes.

## Compliance with Ethics Guidelines

**Conflict of Interest** Margaret D. Weiss has received speaker and consultant honoraria from Eli Lilly, Purdue, and Shire and Janssen.

Stephanie G. Craig, Gregory Davies and Larry Schibuk declare that they have no conflict of interest.

Mark Stein has received grants from Shire, Pfizer and Alcobra and is on the advisory board of Alcobra.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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