**Sleep and ADHD: adding pieces to the puzzle**

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**HIGHLIGHTS**

* ADHD is associated with sleep alterations
* Our understanding of this link is evolving
* Research is underway to inform the management of sleep issues associated with ADHD

‘‘*Generally, the parents of hyperkinetic children are so desperate over the night problems that the daytime ones pale in significance*”. Laufer and Denhoff, 1957 [1].

Clinicians have been familiar with the relationship between ADHD and sleep problems for a long time, as the above statement attests. By contrast, research on this relationship has lagged behind, as shown in Figure 1, depicting the publications retrieved in Pubmed when searching for “Sleep” and “ADHD”. This may have contributed to the omission of sleep in early diagnostic systems and clinical guidelines on ADHD. For instance, whilst “restless sleep” was listed among the symptoms for diagnosing ADHD in the DSM-III (1980) [2], it was then removed in DSM-III-R (1987) [3] and not mentioned in the DSM-IV(TR) ADHD criteria [4, 5]. Likewise, previous clinical guidelines, e.g., the 2007 ADHD Practice Parameters of the American Academy of Child and Adolescent Psychiatry [6], overlooked the association between ADHD and sleep. However, the past 15 years have seen an exponential rise in studies demonstrating a link between ADHD and sleep, and the relevance of assessing sleep in individuals with ADHD has been highlighted in more recent classification systems (e.g., DSM-5(TR) [7, 8]) as well as guidelines, e.g., the 2019 guidelines of the American Pediatric Association [9]. Importantly, relevant studies have been meta-analytically pooled, confirming the cross-sectional association between ADHD and alteration in subjective and, to a lesser extent, objective sleep parameters (e.g., [10, 11]).

However, the link between sleep and ADHD is complex, and there are many aspects, beyond simple cross-sectional associations, that merit investigation. Melegari and colleagues [12] have added a piece to the puzzle, focusing on the links between sleep and internalising/externalising behaviors during the Covid-19 pandemic. In a sample of 992 children with ADHD, children without sleep problems during the lockdown were rated by their parents with significantly lower scores in internalizing and externalizing behaviors compared to those who maintained or had new onset of sleep problems during the lockdown, with higher effect sizes for internalizing than externalizing behaviors.

Children who had a past history of difficulties falling asleep, daytime sleepiness, and nightmares that had resolved by the start of lockdown had lower internalising scores than those with persistent or new onset of sleep problems. Therefore, mood (internalising) and behavioral (externalising) domains were differentially associated with both specific sleep problems and changes in these sleep problems over time.

# Whilst the study by Melegari et al. [10] addressed an unexplored issue, there are other aspects related to the link between sleep and ADHD that deserve investigation. We summarise here those that, in our view, are the key priorities, acknowledging that the list is far from exhaustive.

# First, the field needs rigorous estimates of the prevalence of sleep disorders in children, adolescents, and adults with ADHD. Population-based registries with diagnostic codes for ADHD and specific sleep disorders are well suited to fill this gap.

# Second, while the bulk of the research has been cross-sectional, we need adequately powered studies with long-follow-up periods to gain insight into the longitudinal links between sleep quality/disorders and ADHD. This body of research will be fundamental to inform preventive strategies and early interventions. Efforts are underway [13] to pool data from longitudinal ADHD cohorts, which provides an ideal opportunity to assess the longitudinal relationship between sleep and ADHD.

Third, the impact of sleep problems on brain function and development, alongside the neurobiological underpinnings of the link between sleep and ADHD, across development and more generally across the lifespan, remain under-investigated. Research in this field has the potential to inform treatment strategies that could tackle both ADHD and sleep impairment.

Fourth, while ground-breaking research [14], more than 20 years ago, pointed to night-to-night variability of sleep patterns in children with ADHD, understanding the genetic and environmental correlates of such variability would offer unprecedented opportunities to better manage sleep problems in these children.

Finally, the number of randomised controlled trials (RCTs) to test pharmacological as well as non-pharmacological interventions for sleep problems in ADHD remain limited [15]. A recent systematic review [14] identified only six RCTs (three from the same group) testing behavioral interventions (an additional pilot open trial [15] was published after the search date of that systematic review). With the exception of one trial where the material related to the intervention was mailed to the participants, all the other trials identified by the systematic review were based on face-to-face delivered intervention. As highlighted by the Covid-19 pandemic, a pressing need relates to the development and testing of interventions that can be delivered digitally to alleviate the burden of overstretched clinical services. Examples of research addressing this need include ongoing work to adapt the online parent-delivered intervention “Better Nights, Better Days”, initially developed for neurotypical children, to children with ADHD [16,17], and the Digital Sleep Support for Children with Attention Deficit Hyperactivity Disorder (DISCA) study [16], a research programme aimed at developing and testing, in a multicentre RCT, the clinical and cost-effectiveness of a digital behavioral intervention for chronic insomnia specifically in children with ADHD. These research programmes will extend the literature showing the efficacy of digital cognitive-behavioral therapy for insomnia (CBT-i) in other paediatric clinical populations, as meta-analysed in [19], as well as digital interventions tackling sleep disturbance in children with ADHD using other therapeutic modalities (e.g., meditation [20]).

Based on a search in clinicaltrials.gov, other RCTs are either ongoing or have been recently completed, mainly testing CBT-i. These RCTs will strengthen the current body of evidence on cognitive-behavioral interventions, complementing the evidence base on the pharmacological treatment of sleep problems in ADHD, mainly focused on melatonin. While there is evidence that this compound is efficacious (at least in the short term) and well tolerated in children, less is known about its effects in adults. Ongoing RCTs in adults should fill this gap.

Therefore, from bench to bedside our understanding of the dynamic relationship between sleep and ADHD is rapidly evolving paving the way to clinical benefits for these children. We look forward to the discovery of further pieces of the sleep-ADHD puzzle.

**FIGURE CAPTION**

**Figure 1. Number of publications/year from a PubMed search on “Sleep AND ADHD.”**

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