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Sleep in adults with ADHD: Systematic review and meta-analysis of subjective and objective studies

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ABSTRACT

Sleep alterations associated with adulthood ADHD are poorly understood. Here, we conducted the first meta-analysis of sleep studies in adults with ADHD. Based on a pre-registered protocol (PROSPERO-CRD42017065407), we searched Pubmed, Ovid and Web of Knowledge databases through August 3rd, 2017, with no language or publication type restrictions, and contacted study authors for unpublished data/information. From a pool of 8812 references, we retained 13 studies. Random-effects models were performed and study quality was rated using the Newcastle-Ottawa Scale. Compared to adults without ADHD, those with ADHD significantly differed in seven out of nine subjective parameters (Standardized Mean Difference, SMD, ranging from 0.56 to 1.55) and two out of five actigraphic parameters [SMD (95% CI): sleep onset latency: 0.80 (0.46–1.14); sleep efficiency: −0.68 (−1.03, −0.34)]. No significant differences were detected for polysomnographic parameters. We conclude that, whereas subjectively reported sleep problems are significantly associated with ADHD in adults and should be systematically screened during the clinical interview, additional research is needed to understand if they are underpinned by objective sleep alterations.

1. Introduction

With a worldwide estimated prevalence of about 5% (Polanczyk et al., 2014), Attention-Deficit/Hyperactivity Disorder (ADHD) is the most commonly diagnosed neurodevelopmental disorder in childhood. Impairing symptoms of ADHD persist into adulthood in about 65% of cases (Faraone et al., 2006), with a pooled prevalence of adulthood ADHD around 2.5% (Simon et al., 2009).

1.1. Sleep in children with ADHD

It is well established that ADHD is frequently comorbid with other psychiatric disorders, including oppositional defiant disorder, conduct disorder, mood and anxiety disorders, and substance use disorders (Faraone et al., 2015). Among other conditions possibly associated with ADHD, in the past decade there has been a mounting interest for the relationship between ADHD and sleep disturbance (Cortese et al., 2013). Meta-analytic evidence (Cortese et al., 2009; Diaz-Roman et al., 2016; Sadeh et al., 2006) based on this increasing body of research shows that, compared to non ADHD controls, children with ADHD present with significantly more subjectively reported sleep problems and, to some extent, also objective sleep alterations, as measured by actigraphy or polysomnography (PSG). Of note, one meta-analysis (Cortese et al., 2009) found that such alterations were not accounted for by comorbid psychiatric conditions or by the pharmacological treatment of ADHD.

1.2. Sleep in adults with ADHD

By contrast, evidence on sleep alterations in adults with ADHD is mixed and has not been meta-analyzed yet. While some studies reported an association between ADHD and sleep onset latency, poor sleep efficiency, high nocturnal motor activity, and restless legs syndrome in adults (e.g., Bogdan and Reeves, 2016; Fargason et al., 2013; Philipsen et al., 2005), others failed to find significant difference in important objective sleep parameters such as sleep latency, number of

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sleep awakenings, and total time in bed (Kooij et al., 2001). The inconsistency among studies may be accounted for by possible confounding factors, such as, among others, different methods to diagnose ADHD and lack of a comparison group in some studies (e.g., Fisher et al., 2014; Langberg et al., 2016).

Given these mixed findings, a meta-analysis that takes into account possible confounding factors is timely to elucidate if and to which extent ADHD is significantly associated with subjectively reported and/or objectively measured sleep alterations, possibly replicating findings from children. Indeed, given developmental changes in sleep patterns and ADHD symptoms, it should not be assumed that sleep findings in children are necessarily identical to those in adults with ADHD.

The focus on sleep in individuals with ADHD is of relevance for the management of ADHD. Such problems can be a significant source of distress for the patients and their families (e.g., Hvolby et al., 2008; Owens et al., 2000; Owens et al., 2013). They may also worsen or mimic symptoms of ADHD (Dahl, 1996). Therefore, the appropriate assessment and treatment of sleep problems might improve the quality of life of individuals referred for ADHD assessment and reduce the severity as well as the impairment of ADHD. However, in order to appropriately manage sleep complaints in patients with ADHD, it is necessary to better characterize their profile and understand the specific sleep alterations underlying these complaints.

Here, we conducted the first systematic review with meta-analysis of studies reporting subjective or objective sleep parameters in adults with a diagnosis of ADHD according to standardized criteria for the diagnosis of ADHD. Give the exploratory nature of this meta-analysis, no *a priori* hypotheses were formulated.

2. Method

We followed the recommendations of the Meta-Analysis of Observational Studies in Epidemiology group (Stroup et al., 2000) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009). The protocol of this systematic review was registered in PROSPERO (CDR 42017065407). Data were extracted from the published reports (journal article) of the studies, or obtained by study authors. The PRISMA checklist is reported in the Supplemental material 1.

2.1. Types of studies

Case-control studies comparing subjective and/or objective sleep parameters in adults with and without ADHD were included.

2.2. Types of participants

2.2.1. Inclusion criteria

Studies on adults (≥18 years) with a diagnosis of ADHD established according to the *International Classification of Diseases* (ICD) (any version) or the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) (any version) were eligible. Studies had also to include a comparison group of adults without ADHD.

2.2.2. Exclusion criteria

We excluded studies where participants presented with ADHD symptoms above a specific cut-off in ADHD scales, without meeting formal criteria for ADHD as per DSM or ICD criteria.

2.3. Outcomes

Any subjective sleep parameter from any sleep questionnaire (e.g., sleep onset latency, psychosomatic symptoms during sleep onset, sleep duration, night awakenings, sleep quality, sleep efficiency, restorative value of sleep (i.e., feeling rested after waking up), daytime sleepiness, general sleep problems) and/or any objective sleep parameter (e.g., actigraphy: sleep onset latency, true sleep, assumed sleep time, actual wake time, sleep efficiency; PSG: sleep onset latency, stage 1 sleep %, stage 2 sleep %, slow wave sleep %, REM %, REM latency, total sleep time, sleep efficiency, wake time %) were eligible. We included any parameter present in at least two studies.

2.4. Search strategy/syntax

The following electronic databases were searched until August 3rd, 2017, with no language/date/type of document restrictions: Pubmed (Medline), Ovid databases (PsycInfo, Embase + Embase classic, Ovid Medline), and Web of Knowledge databases (Web of science (Science Citation Index Expanded), Biological abstracts, Biosis, Food science and technology abstracts). Additional details on the search strategy/syntax, including search terms for each database, are reported in the Supplemental material 2. References of included studies were scanned to find any potential pertinent study detected with the electronic search.

2.5. Study selection

Retrieved references were independently screened and blindly double-coded for eligibility by two study authors. Any disagreement was resolved by a senior author. If needed, study authors were contacted to gather missing/additional information.

2.6. Study quality/bias assessment

Study quality was assessed using the Newcastle-Ottawa Scale for case control studies (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) focusing on the following items: case definition, representativeness of the cases, selection of controls, definition of controls, comparability of cases and controls on the basis of the design or analysis, ascertainment of exposure, non-response rate.

2.7. Data extraction and statistical analysis

Data extraction was performed blindly by two of the authors, and any discrepancy between the two was resolved by consensus with a third senior author. We contacted study authors when necessary. Data extracted from each study included: first author, publication year, country where the study was conducted, participants details (number, age, sex, medication use, ADHD subtypes, and comorbidities), sleep measures (mean, SD), and study key findings.

Random-effects models were used to compute effect size for each sleep variable. We calculated the standardized mean difference (SMD), with 95% confidence interval (CI), with the correction of Hedges (Hedges, 1981) to avoid bias due to sample size. The pooled SMD, and related 95% CI, was calculated through the inverse variance method, and its statistical significance was assessed by the Z statistic. I^2 (Higgins and Thompson, 2002) was calculated to quantify heterogeneity among studies. Finally, Egger's test (Egger et al., 1997) and funnel plots were used to evaluate publication bias. Analyses were performed using Review Manager 5.3 (http://community.cochrane.org/tools/review-production-tools/revman-5) and Comprehensive Meta-Analysis (https://www.meta-analysis.com/) software.

3. Results

3.1. Studies included in the meta-analysis

From a pool of 8812 non-duplicate potentially relevant references, 13 studies (Arns et al., 2014; Baird et al., 2012; Bioulac et al., 2016; Boonstra et al., 2007; Brevik et al., 2017; Frye et al., 2017; Kooij et al., 2001; Philipsen et al., 2005; Sobanski et al., 2008, 2016; Tonetti et al., 2017; Van Veen et al., 2010; Weibel et al., 2017) were retained for the