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Sleep in Childhood Attention Deficit Hyperactivity Disorder

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Abstract

Background

Sleep impairments frequently co-occur in children with Attention Deficit Hyperactivity Disorder (ADHD), and the nature of their relationship is bidirectional. Sleep problems in this population manifest as difficulties falling asleep, maintaining sleep and in poorer sleep quality, greater daytime sleepiness, altered sleep duration and increased limb movement in sleep. These concerns affect the quality of life, academic performance, cognitive functions, behavioural and family health of the child, negatively impacting their functional outcomes. Early identification and management of sleep problems in this population therefore has deep-rooted clinical utility. In this thesis we aimed to comprehensively delineate the nature of sleep problems in children with ADHD, explore the possible ADHD related cognitive/behavioural facets and environmental factors that might be influencing the child's sleep and translate our understanding to the design of ADHD-specific sleep assessment tool for clinical utility.

Methods and Results

Chapter 2 reports the systematic review of studies investigating sleep in children between the age of 5-13 years who are diagnosed with ADHD. 148 empirical studies published between 2009-2019 were reviewed and a narrative synthesis was presented categorising studies into five sections. These included studies exploring the nature of these difficulties (subjective reports, sleep macrostructure and microstructure); studies exploring circadian rhythm patterns in this population, consequences of sleep problems, non-pharmacological interventions affecting sleep and ADHD symptoms, and pharmacological interventions affecting sleep in this population. We found that sleep disturbances may worsen behavioral outcomes; moreover, sleep interventions may improve ADHD symptoms, and pharmacotherapy for ADHD may

impact sleep. Gaps in research focussed on the need for using mixed methodologies utilizing objective and subjective reports of sleep, designing well powered studies that define the role of sleep in ADHD clinical picture and facilitate assessment and management of sleep problems.

Chapter 3 qualitatively investigated the nature of sleep problems and sleep related behaviours in children with ADHD. 26 parents of children diagnosed with ADHD aged between 6-12 years were interviewed about their child's sleep. Thematic analysis of the interviews generated three broad themes which revolved around facets of children's sleep difficulties as perceived by parents, the perceived impacts of these difficulties, and steps taken by parents to improve their child's sleep. Parents expressed that sleep problems can be a significant disruptor for their children's functioning and the wider household. Parents reported using need-based individualised behavioural and sleep hygiene approaches to counter their child's sleep problems.

Chapter 4 examined the associations of parent-rated sleep problems and sleep timings of pre-adolescent ADHD children with parental insomnia symptoms, ADHD (screener based) features and dysfunctional attitudes and beliefs about sleep (in 120 parent-child pairs). 82% of children exceeded the threshold for a paediatric sleep disorder, and parental insomnia, ADHD symptoms and dysfunctional beliefs about sleep were associated with childrens's sleep problem scores, and with the subfactors of sleep anxiety and parasomnias. Sleep was poorer for children whose parents were both insomnia probable and had ADHD consistent features, thereby underlying the significant double impact of both on the child.

In Chapter 5, a thirty-five-item parent rated sleep problems questionnaire for children with ADHD was developed. This questionnaire, called Childhood ADHD Sleep Scale (CASS), included 5 domains: Bedtime, Behaviours in Sleep, Sleep Quality, Daytime Functions and Impacts on Family, where the respondent has to choose one out of five options for a sleep

problem statement (‘strongly agree’, ‘somewhat agree’, ‘neither agree or disagree’, ‘somewhat disagree’, and ‘strongly disagree’). CASS showed acceptable test-retest reliability and good internal consistency. Exploratory factor analysis of the CASS generated the 4-factor reduced CASS including sleep problems and impacts, executive and sensory regulation, daytime functions, and parasomnias. The reduced CASS demonstrated good test-retest reliability and internal consistency. Both unreduced CASS and reduced CASS were compared with scores from Child Sleep Habits Questionnaire (CSHQ) and Brown Executive Functions and Attention Scales (Brown -EFA). Differences in the trends of associations were discussed, to understand the utility of an ADHD specific sleep assessment questionnaire.

In Chapter 6, we used an emotional Stroop test to assess the presence of sleep related attentional bias in 155 young adults and examined whether their Stroop test performance and sleep bias scores would associate with their ADHD screener-based symptom scores. Sleep quality scores, insomnia probability scores and social jetlag and chronotype. ADHD consistency scores, and insomnia probability scores were not found to be associated with sleep attentional bias scores. Sleep attentional bias also did not associate with chronotype or social jetlag, but it was found that habitual use of alarm clocks on workfree days did associate with greater sleep attentional bias, indicating that curtailed sleep due to functional demands on these days might increase attention towards sleep related stimulus.

Conclusion

This thesis highlighted how sleep functioning manifests in the clinical picture of childhood ADHD. The bidirectional relationship between the two entities were explored through varied methodological approaches to draw associations between the child’s environment, their own neurodevelopmental diversity and the accompanying sleep features that define their ADHD specific sleep functioning. We aimed at creating a framework within

which sleep problems in ADHD can be understood and utilized for clinical utility, both in terms of assessment and management of these concerns. We also found that social demands can enhance cognitive processing of sleep related stimulus in older cohorts with or without ADHD features.

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List of Abbreviations

AD	Alzheimer's Disease
ADHD – C	Attention Deficit Hyperactivity Disorder Combined presentation.
ADHD – I	Attention Deficit Hyperactivity Disorder Inattentive presentation
ADHD	Attention Deficit Hyperactivity Disorder
ADHD- H	Attention Deficit Hyperactivity Disorder Hyperactivity/Impulsivity presentation
AHI	Apnea-Hypoapnea Index
ANOVA	Analysis of Variance
ANS	Autonomic Nervous System
ASD	Autism Spectrum Disorder
ASPS	Advanced Sleep Phase Syndrome
ASRS	Adult ADHD Self Rating Scale
AUCg	Area Under the Curve ground
AUCi	Area Under the Curve increase
BIS	Barratt Impulsivity Scale
BMAL1	Brain and Muscle ARNT-Like 1 protein
Brown EFA	Brown Executive Functions and Attention scales
CAP	Cyclic Alternating Pattern
CAR	Cortisol Awakening Response
CASS	Childhood ADHD Sleep Scale
CBTi	Cognitive Behaviour Therapy for insomnia
CCGs	Clock Controlled Genes
CCTQ	Children's Chronotype Questionnaire
CD	Conduct Disorder
CEN	Central Executive Network
CGI	Clinical Global Impression
CLOCK	Circadian Locomotor Output Cycles Kaput
CPT	Continuous Performance Test
CRH	Corticotropin releasing hormone.
CRY	Cryptochrome
CSAS	Central Sleep Apnoea Syndrome
CSHQ	Child Sleep Habits Questionnaire

CSWS	Child Sleep Wake Scale
DA	Dopaminergic
DBAS	Dysfunctional Beliefs and Attitude about Sleep
DMN	Default Mode Network
DNA	Deoxyribonucleic Acid
DSM - V	Diagnostic and Statistical manual of Mental Disorders – Fifth Edition
DSPS	Delayed Sleep Phase Syndrome
EFA	Exploratory Factor Analysis
ERPs	Event Related Potentials
FISH	Family Inventory of Sleep Habits
GABA	Gamma Amino-butyric Acid
GRP	Gastric- Releasing Peptide
HD	Huntington's Disease
HPA	Hypothalamic Pituitary Adrenal
ipRGC	intrinsically photoreceptive Retinal Ganglion Cells
IQR	Inter Quartile Range
LC	Locus Coeruleus
LDX	Lis dexamphetamine
MANOVA	Multivariate Analysis of Variance
MAXQDA	Max Weber Qualitative Data Analysis
MCTQ	Munich Chronotype Questionnaire
ME score	Morningness – Eveningness score
MPH	Methylphenidate
MSF	Mid Sleep on Free days
MSLT	Multiple Sleep Latency Test
MSPSQ	Modified Simonds and Parraga Sleep Questionnaire
MST	Motor Sequence Task
MSW	Mid Sleep on Workdays
NE	Norepinephrinergic
NHE	Naples High Excitability
NPAS2	Neuronal PAS Domain Protein 2
NREM	Non-Rapid Eye Movement
OCD	Obsessive Compulsive Disorder
ODD	Oppositional Defiant Disorder

OSA	Obstructive Sleep Apnoea
PD	Parkinson's Disease
PER	Period
PLMI	Periodic Limb Movement Index
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
PRS	Polygenic Risk Scores
PSG	Polysomnography
PSQI	Pittsburg Sleep Quality Index
RCT	Randomised Controlled Trial
RCT	Randomised Controlled Trial
REM	Rapid Eye Movement
RHT	Retinohypothalamic Tract
ROR	Retinoic related Orphan Receptors
RT	Reaction Time
SCI	Sleep Conditions Indicator
SCN	Suprachiasmatic Nucleus
SDSC	Sleep Disturbance Scale for Children
SHIP	Sleep Hygiene Inventory Paediatrics
SHR	Spontaneous Hyperactive Rat
SJL	Social Jetlag
SpO2	Saturation of Peripheral Oxygen
SRBD	Sleep Related Breathing Disorder
SWA	Slow Wave Activity
SWS	Slow Wave Sleep
TA	Thematic Analysis
TMN	Tuberomammillary Nucleus
TST	Total Sleep Time
TTFL	Transcriptional- Translational Feedback Loop
VIP	Vasoactive Intestinal Peptide
VLPO	Ventrolateral Preoptic nucleus
WISC III	Wechsler Intelligence Scale for Children – Third Edition
WISC IV	Wechsler Intelligence Scale for Children – Fourth Edition

Publications arising from this thesis.

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Prologue

'It would be pointless for a plum blossom to try to remake itself as a cherry blossom, no matter how deeply the plum yearns to do so. The plum is happiest when it blooms as itself in full glory. How much of the colour and wonder of life would be lost if it weren't for our differences.'- Daisaku Ikeda.

Frank is a cheerful nine-year-old boy, currently enrolled in primary school, who seems to be imaginative and humorous. In a consultation with a psychologist, his parents reported being concerned about their son's academic performance and certain aspects of his behaviour. As conveyed by his schoolteachers, staff and by his mother, Frank exhibits certain disruptive behaviours within the classroom/the school premises and sometimes in social gatherings. These behavioural reactions are not resulting from any apparent emotional concerns such as anger but are for the most times playfully or accidentally occurring due to lack of control in Frank over his own reactions. He also exhibited having difficulty sitting still in the class or paying attention during lessons and tends to move around. Some difficulties with interpersonal relationships among peers are experienced by Frank, causing difficulties in maintaining friendships with classmates. Further as reported by his parents, Frank has been facing some academic concerns in certain subjects, especially English and Math. To shed light upon the reasons behind these concerns, a comprehensive psychological assessment was planned for Frank, which would entail examining his level of cognitive ability, academic achievement, neuro-psychological functioning, phonological processing, and social-emotional functioning.

Systematic examination of Frank's psychological test results, clinical observation and interview coupled with the detailed clinical history and information gathered from him, his parents and teacher, indicates that Frank possesses an average intellectual ability with a below average academic functioning level in the domain of Mathematics, coupled with clinically

significant difficulty in paying selective attention and lack of age appropriate behavioural inhibition, that are leading to a somewhat substantial level of concerns in his school performance and functioning in social environments. Frank met the criteria to warrant a diagnosis of ***Attention Deficit Hyperactivity Disorder (ADHD)*** *- Combined presentation as per the Diagnostic and Statistical Manual of Mental Disorder- Fifth Edition (DSM-V).*

Although Frank's primary difficulties were directly related to inattention and difficulty controlling his bodily reactions, upon careful evaluation of his functioning, majority of his disturbances could be interlinked to his day-to-day functioning and especially to that of his sleep. Therefore, to describe Frank's ADHD clinical presentation, an extent of the focus must be inevitably directed to his overall lifestyle. The detailed interview presented, that at home Frank would generally start doing his homework late after dinner and would refuse to go to bed consistently. This refusal has led his parents to design most of the work at home towards the later part of the night. Frank generally goes to bed around midnight on schooldays and wakes up after a lot of effort at 7 am in the morning to leave for school. Most of the days in the morning Frank misses his breakfast and forgets to carry the notebooks and texts to school that are required for lessons. At school he generally gives the reason that he was asking a classmate for a text/notebook during a lesson, when he is found chatting with others and moving around in the class. By recess, Frank partially finishes his lunch to join his friends for free play. By the later afternoon, teachers report Frank seems irritable and sleepy. While the class dispersal takes place, almost every day Frank ends up in a physical fight with the student standing in front or behind him in the file. This is the daily picture for Frank within school. The above reported events demonstrate that although Frank was found to have clinically significant inattention and hyperactivity, his day-to-day functioning has been strongly influenced by them and have formed a pattern in his psychological and physiological functioning, especially in his cycles of rest and activity. Therefore, for an individual demonstrating features of ADHD, their

Circadian System has a crucial involvement in forming patterns of behaviour that in turn describes their clinical presentation of ADHD symptoms. Substantial literature till date has demonstrated the presence and influence of sleep concerns/ deviation of sleep parameters among children diagnosed with ADHD. This thesis attempts to elucidate how differences in sleep/wake patterns among children diagnosed with ADHD can influence the clinical characteristics of the condition; its impact on the child and their environment; and how a comprehensive account of these differences can be utilised therapeutically to enhance the child's functioning. We start by describing the major features of ADHD and extend our discussion to the researched areas of deviation observed in the pathophysiology of ADHD that embodies differences in circadian functioning.

Chapter 1:
Introduction

Parts of this chapter have been published as:

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1.1 Attention Deficit Hyperactivity Disorder

Both in research and practice, the thought of ADHD evokes the quintessential features of inattention and/or hyperactivity/impulsivity, although the manifestation of these features can be experienced in varied spheres of the individual's functioning. The Diagnostic and Statistical manual of Mental Disorders (DSM-V) describes ADHD as a neurodevelopmental disorder that is characterized by a persistent pattern of inattention and/or hyperactivity/impulsivity that interferes with functioning or development (APA,2013). Table 1.1 describes the symptoms and manifestations of ADHD in everyday life.

Table 1.1

The symptoms of ADHD can be understood best functionally through the following table.

Symptom	Manifestation (APA, 2013)	Examples of functional implications
Inattention	Wandering off tasks; lacking persistence; having difficulty sustaining focus; being disorganized.	Makes careless mistakes; does not read instructions carefully; leaves the reverse side of the test unanswered; quickly gets bored; appears dreamy or preoccupied; non efficient planning; arriving late; postpone tasks so that deadlines are missed; mislays wallet/key/important items; loses notes; easily distracted by noises; difficulty filtering information.
Hyperactivity	Excessive motor activity when it is not appropriate; excessive fidgeting; tapping or talkativeness.	Difficulty sitting still (avoids symposiums, lectures church etc); fiddling with hair; biting nails; feeling restless/agitated; difficulty in speaking softly; climbing furniture/tress; unable to watch TV/films quietly; not giving room to others to interject in a conversation; constantly busy; has lots of energy; always on the go.

Impulsivity	Hasty actions/importantdecisions that happen in themoment without forethought; potential to cause harm to the individual; inability to delay gratification; social intrusiveness.	Impulsively commencing/ending relationships; lots of arguments; left work for argument/dismissal; low self-assertiveness because of negative experience; few friends; being a bully/being teased; injuries as a result of excessive sport/risky recreational activities.

ADHD is associated with impairment across various spheres of functioning, which include academic achievement, age appropriate interpersonal/social skills, personal health/safety, parenting and occupational outcome (Noggle et al. 2012). It is a brain-based disorder which usually emerges in childhood that sometimes continues through adulthood (Noggle et al 2012) causing a significant magnitude of detrimental consequences for the individual as well as for the community as a whole (McGough, 2014).

1.2 Major behavioural manifestations

Behavioural manifestation of ADHD in the preschool child often includes poor intensity of play and increased motor restlessness with motor & speech developmental delays, defiant behaviour and lower than age-appropriate social skills (Alessandri 1992; DuPaul et al 2001). Specific support for carers is crucial to avert high stress often due to the child not responding to ordinary parental requests (DuPaul et al 2001; Barton 2002). For the child in primary school, deviation from typically developing functionality becomes evident when the child demonstrates academic failure (due to attentional deficits and comorbid learning difficulties), rejection by peers and low self esteem in the school environment and difficulty in managing behaviours by carers in the home and social environment (Bagwell et al 2001). Due to persistent problems related to sleep patterns, the child might refuse to follow bedtime routines, or sleep at pre-designated times, thereby the parents having to change their evening

schedule to look after the child (Johnston & Mash 2001; Sciberras et al 2015).

Morphological and functional deviations in the ADHD brain and the objective/subjective account of ADHD symptomatology have pointed towards deficits of executive control. Executive dysfunction in the ADHD clinical picture is most clearly manifested in the form of a lack of inhibitory control. Inhibitory control can be described as processes that effect information selection at the time of attentional processing and choosing between conflicting situations (or actions) that requires the individual to suppress less dominant incongruent information (Konicarova, 2018). For example, in a Neuropsychological test of inhibitory control such as NEPSY-II the child must supress the urge to consider saying the actual colour of the target shape, rather than the test trial rule where in they must say the opposite colour (black for white or white for black). Further studies have shown that ADHD features are mainly concerned with two types of deficits in executive control: cognitive deficits, related to the attentional concerns, and affective deficits, related to altered emotional reactions. Here the role of an over-excitable limbic system has been postulated (Castellanos et al. 2006; Toplak et al. 2005; Antonini et al. 2015; Martinez et al. 2016). Therefore, ADHD symptoms may be a result of not only the executive function concerns of the frontal cortex, but also disrupted functioning and structural features of the subcortical brain regions such as those of the limbic system.

Comorbid psychological problems are highly prevalent in ADHD, with the childhood population often presenting complex combinations of learning disorder, oppositional defiance, conduct disorder, anxiety disorder, Autism spectrum disorder and affective disorder features (Bartholomew & Owens 2006). The presence of varying degrees of the above comorbidities, coupled with learning difficulties and lack of preacademic skills, can lead to a host of interpersonal and academic challenges in children with ADHD (Barkley, 1998; Mariani & Barkley 1997 & Shelton et al 1998).

1.3 Developmental trajectories in the ADHD clinical picture

The clinical picture of ADHD is substantially heterogenous, with a wide range of severity in core symptom presentation, which also overlap with other conditions (including not only psychiatric, but somatic diseases and physiological states as well; Poirier et al., 2016). The clinical presentation of ADHD depends on the developmental stage of the individual (Franke et al 2018). Due to its complex clinical presentation, the DSM-5 (and its preceding versions) proposed the need to define core signs, age of onset, course, and count of symptoms, to warrant a clinical diagnosis. But because ADHD is not only assessed at childhood, looking at the condition from a lifespan perspective becomes relevant to avoid misdiagnosis, oversimplifying and generalizing the clinical picture and the resultant management plan.

1.3.1 Age related changes

Differentiating the core symptoms of ADHD according to age, shows that adults show reduced signs of motor hyperactivity, individuals in middle childhood might display comparatively more inattentive symptoms (which continues into adulthood), and young children are more likely to demonstrate externalising features such as hyperactivity/ impulsivity (Francx et al., 2015; Willcut et al 2012). ADHD has essentially been characterised as a childhood- onset neurodevelopmental disorder, with the symptoms having to be present before the age of 12 years as per the DSM-5 (APA, 2013). Older age onset symptoms could be due to brain injuries, in which case the ADHD would be 'secondary' to the predominant condition, however this might be clinically indistinguishable from idiopathic ADHD (Schachar et al 2015), therefore making this a controversial topic. Adult onset ADHD could also be due to the existence of subthreshold childhood ADHD (Faraone & Biederman 2016).

1.3.2 Comorbidities

The ADHD clinical picture is highly associated with comorbid psychiatric and non-psychiatric conditions (Angold et al 1999), and the patterns of these comorbidities change substantially over an individual's lifetime (Taurines et al 2010). Although not an exhaustive account, Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD) are frequently associated comorbidities in the childhood clinical picture, Substance Abuse Disorder, Anxiety Disorder, Mood disorders and sleep disorders might be more prevalent in adulthood (Jacob, et al 2007). Significant literature and clinical practice acquired information has demonstrated the presence of Autism Spectrum Disorder (50-70%, Hours et al 2022), Tics Disorders (7%, Ogundele and Ayyash, 2018) and learning disorders (54%, Büber et al 2020) as other prevalent comorbidities in ADHD (Rommelse et al 2011; Roessner et al 2011; Sciberras et al 2014). High levels of comorbidity between ASD and ADHD due to potential sharing of underlying genetic predisposition (for example SHANK2 pleiotropic gene) has been implicated (Ma et al 2021).

1.4 Prevalent Management Pathways

As per the NICE 2018 guidelines, the management/treatment strategies vary across the age groups. While ADHD-focused parent groups are the first line of treatment for children below the age of 5 years, and medication is not recommended in this age group without secondary specialist advice, for young children above the age of 5 years psychosocial interventions and environmental modifications is the first line of treatment, pharmacotherapy/ together with cognitive behavioural therapy is the second line of treatment; and for adults pharmacotherapy is the first line of treatment. Traditionally divided into two groups, pharmacological interventions involve either stimulants or non-stimulants, with Methylphenidate and Amphetamine as the stimulant medication, and Atomoxetine, Guanfacine and Clonidine as the non-stimulant options (Faraone et al 2015).

1.5 ADHD Epidemiology:

Thomas et al. (2015), in their meta-analysis estimated the worldwide ADHD prevalence rate of 7.2% among childhood with higher values ranging from 8.7%-15.9% for community-based samples. In the Republic of Ireland, the Child and Adolescent Mental Health Services (CAMHS) reported in their fifth annual report (2014) that for 31.6% of young referrals, ADHD was their primary diagnosis. While there is some variability in severity and comorbidity, a significant proportion of those diagnosed in childhood are likely to meet the diagnostic criteria or struggle as a result of ADHD during adult life (Van Lieshout et al., 2016; Uchida et al., 2018). With a consistent increase in the prevalence of ADHD rate overall amidst debates over how much of the increased diagnoses can be attributed to true increases in frequency, improved detection, or diagnostic inflation because of misdiagnosis and/or overdiagnosis (Kazda et al. 2021), the above figures are constantly changing every couple of years.

With respect to gender differences, while males are more likely to demonstrate elevated symptoms,and thereby are more likely to receive a diagnosis during the childhood, females tend to show increase in symptoms during early adolescence (Murray et al 2019). Therefore, among the child population, ADHD is diagnosed in males than in femaleswith a sex ratio of 3:1 (Willcutt, 2012), which during adulthood evens out to 1:1 (e.g. Williamson & Johnston, 2015).

1.6 The ADHD brain and Cognition: Past findings and recent directions

ADHD has been a subject of investigation since the beginning of the 20th century, when Still (1902), described an 11-year-old hyperactive boy who displayed ‘loss of moral control’ and ‘psychical disturbance’. A detailed description of symptoms including hyperkinetic behaviour and loss of motor inhibition were included in his lecture.

Frank et al (2018) stated that cognitive impairments are at the core of ADHD with higher level effortful cognitive functions (such as inhibitory control and working memory) and those cognitive processes which are of an automated nature, such astemporal information processing and timing, vigilance and reward processing(Karalunas et al., 2014; van Lieshout et al., 2013; Willcutt et al., 2005). These problems have also been reported among children (Huang-Pollock et al., 2012; Willcutt et al., 2005).

In 1972, Douglas described the positive effects of Methylphenidate on the symptoms of inattention and hyperactivity. The core symptoms characterising ADHD (inattention, hyperactivity, and impulsivity) have been presented in research and clinical practice guidelines (such as ICD-10 and DSM-V) quite consistently, with only minor alterations in contemporary guidelines. However, brain related structural and functional dysfunctions associated with ADHD have seen plenty of turns and novel outlooks since the past few decades. Mattes in 1980's argued that the dysfunctions in the frontal lobe regions are related to ADHD. Niedermeyer and Naidu (1997) further validated that disinhibition of motor activity and features of inattention observed in ADHD resulted from a 'lazy' rather than a damaged frontal lobe. Although certain structures of the brain play a more pronounced role in the aetiology of the disorder, studies have pointed towards the total reduced volume of the brain in ADHD individual to be most likely linked to the condition (Castellanos and Proal, 2012). Cortical thinning has been reported in the medial and dorsolateral prefrontal cortex (consisting of networks supporting attention), which is related to deficits in attentional capacity from young childhood to adulthood (Shaw et al., 2013). Specifically, studies have found decreased volumes of corpus striatum, prefrontal cortex, corpus callosum and cerebellum to be linked to the characteristic levels of cognitive and emotional functioning observed in ADHD (Seidman et al. 2005; Nigg 2001; Castellanos et al. 2006; Valera et al. 2007; Castellanos and Proal 2012). Plessen and his colleagues (2006) suggested the involvement of the limbic system in the

pathophysiology of ADHD, and have attributed executive function concerns such as lack of processing speed, time management and excessive stimulus seeking behaviors in ADHD to enlarged hippocampus among children and behavioural disinhibitory tendencies to dysfunctional connections between the amygdala and the orbitofrontal cortex. Impairments in Event Related Potential (ERPs) have been related to selective attention, inhibition and response preparation in continuous performance tasks (Doehnurt et al., 2013).

Maturational dysregulation of the frontal lobe connections have been implicated in ADHD, with underdevelopment of several feedback loop pathways that control motor function (Leisman and Melillo, 2022), where circuits travel from a particular area of the cortex to the basal ganglia, going on to the thalamus and returning back to the cortex (Sherman, 2011). In ADHD, overactivity of the left hemispheric connections to the direct pathways is linked to underdevelopment of the right hemisphere (Chen et al 2016). One of these networks is the Default Mode Network (DMN), active during daydreaming and unfocused behaviour (Gusnard and Raichle, 2001). It has been indicated that ADHD individuals have greater gray matter in the DMN nodes, so when completing a task, the DMN infringes on the cognitive system that is necessary to complete the task (Rubia et al 2014). Another network is the Central Executive Network (CEN), crucial for working memory tasks, rule-based problem solving and decision making (Schneider and Shiffrin, 1977) is more focused on the left as well as more towards the external environment (Silk et al 2016) which is overactive in ADHD (Bilevicious et al 2018).

Another line of investigations has focussed on the role of dysfunctional catecholamine secretion in ADHD. Animal studies have demonstrated abnormality of the dopaminergic (DA) and norepinephrinergic (NE) systems in ADHD. The rodent study involving the Spontaneous Hypertensive Rat (SHR) showed reduced level of Dopamine in the prenatal SHR mid brain regions and heightened Dopamine transporter activity in the adult SHR (Watanabe et al 1997; Leo et al 2003 & Russell 2007). These studies also emphasize on whether ADHD

pathophysiology is a result of a hyperdopaminergic or a hypodopaminergic tendency. In 2003, Vagianno and his colleagues demonstrated low motor activity in gene-knockout model mice who lacked the DA transporter or Tyrosine Hydroxylase. These mice were observed to be more hyperactive in novel situations and appeared less active on administration of stimulants. This study inclines towards the hyperdopaminergic model of ADHD. The same authors also studying the Naples High Excitability (NHE) rat,(a strain showing signs of hyperactivity and poor working memory) and found increased staining of the DA transporter in the pre-frontal cortex. On the other hand, the SHR model displayed low levels of DA in the ventral tegmental, substantia nigra and the caudate nucleus areas and more release of DA in the prefrontal cortex and nucleus accumbens (Adriani et al 2003). In addition to an inclination towards hypo DA hypothesis, this study suggested the possibility of an impaired DA storage function implicated in ADHD.

Grace (2001) explained the complex relationship through which the hypo and hyper dopaminergic presence could lead to the psychopathological manifestations of ADHD. Optimal transfer of neuronal information is due to phasic release of Dopamine; however, in ADHD the tonic pool is reduced and this in turn leads to excessive phasic release of Dopamine. This excess in turn over-stimulates the reward centres in the nucleus accumbens, leading to disorganised executive function. The behavioural consequence is a significantly increased sensory seeking tendency. Stimulants such as Methylphenidate, block the re-uptake of DA, and increases the size of the tonic pool, which in turn regulates the phasic release (Grace,2001).

1.7 Interplay of gene and environmental risk factors in ADHD

ADHD has a strong genetic component, with family studies demonstrating 10 times the prevalence of the disorder in first degree relatives of ADHD candidates (Biederman et al 1990; Frank et al 2012) and up to 80% heritability among twins (Faraone et al., 2005). ADHD is of

polygenic nature, where genetic investigations are mostly are hypothesis driven gene association studies and genome wide association studies (Anney et al., 2008; Sanchez-Mora et al., 2015; Yang et al., 2013 & Zayats et al., 2015). A number of studies have used the polygenic risk score (PRS) method to estimate the genetic liability for ADHD that can be ascribed to identified genetic polymorphisms; the PRS accounts for small percentage of the liability for ADHD (<5%), indicating that the majority of the genetic liability for ADHD remains undescribed (Torkamani et al., 2018; Martin et al 2019; Ronald et al 2021). ADHD PRS has been significantly related to ADHD dimensional scores, parent, teacher and self-reports (Albaugh et al 2019; Burton et al., 2019; Nigg et al., 2020; De-Zuew et al 2020).

Literature has also shed light upon the variability in gene expression, (thus influencing the phenotypic trait), influenced by the environment and other epigenetic factors (Balogh et al., 2022). Environmental risk factors for ADHD, such as maternal substance abuse, environmental toxins during pre-natal and perinatal periods, suboptimal nutritional factors and presence of psychosocial stressors during early childhood have been implicated in ADHD risk, and increased stress, trauma and abuse during adolescence can contribute to epigenetic modification (Loche & Ozanne, 2016 Variations in specific genes might themselves lead to increased vulnerability to ADHD: for example, dopamine receptor D4's interaction with maternal smoking (Pluess et al., 2009), dopamine transporter receptor's interaction with maternal alcohol consumption (Brookes et al., 2006), or an interaction between Serotonin transporter genotype (5HTT) and adverse psychosocial events (Palladino et al., 2019). Current literature supports the notion of ADHD as a trait-based condition, where symptoms are present along a dimensional spectrum (with ADHD being nested in one unipolar position, present in substantial intensity), rather than its absolute presence or absence (Larsson et al., 2012).

1.8 ADHD Outcomes with and without treatment

Numerous randomised controlled trials (RCT) and meta-analyses have documented evidence base for pharmacological treatment for ADHD with stimulants (methylphenidate and amphetamine formulations) and non-stimulant medication (atomoxetine) (Wolraich et al 2011). Psycho-social treatments include parent training, classroom management, behavioural techniques, and peer-based interventions, either provided independently or combined with pharmacotherapy (Pelham and Fabiano, 2008).

High quality clinical studies in pre-adolescents, adolescents and adults with ADHD have consistently demonstrated poorer outcomes in academic, occupational, and social functioning associated with ADHD compared to typically developing cohorts (Klein et al 2012). A Scandinavian register-based studiy has shown higher mortality rates in ADHD, related to deaths from unnatural causes such as accidents (Dalsgaard et al 2015); such findingsare supported by previous literature (Chang et al 2014). Following effects of long-term pharmacological treatment, register based studies have shown decreased criminality (Lichtenstein et al 2012) and reduced traffic accidents (Chang et al 2014), which has been validated also in a US population (Chang et al 2017). Risk-to-benefit ratio debates have long been associated with use of stimulant medication for children with ADHD. There is mixed evidence regarding the effects of stimulant medication on children's growth (Mattes et al 1983; Lisska & Rivkees 2003; Klein & Mannuzza 1988; Biederman et al 2003); concerns regarding risk of later-in-life drug abuse (Biederman et al 1998; Skoglund et al 2015) and risk of depression (Chang et al 2016, Man et al 2017) have come to surface. Among children, pharma-epidemiological investigations (Dalsgaard et al 2015; Man et al 2015 & Mikolajczyk et al 2015) have revealed reduced risk for injuries and subsequent decreased ward visits. Regarding care and management of individuals with ADHD, increased healthcare costs have been

consistently estimated through studies, related to increased risk of injuries, substance abuse, higher incidence of mental health problems and increased stress (Leibson et al 2001; DiScala et al 1998; Sullivan & Rudnik-Levine 2001; Schubiner et al 2000; Swensen et al 2003; Brown & Pacini 1989).

1.9 Circadian Rhythms

In 1729, the French astronomer Jean Jacques d'Ortous de Mairan observed that the Mimosa plant unfolds its leaves during the day and closes them during the night in both light and constant dark conditions (Foster & Kreitzman 2004). In anticipation of the day-night cycle induced environmental changes, living organisms adapt their behaviour via endogenous oscillators, thereby creating near-about 24 hours circadian rhythms (Wulund and Reddy, 2015). As such, the circadian clock is a product of an evolutionary process where in the selection of the fittest was based on finding an optimally cyclic predictable environment. Pittendrigh (1960) defined circadian rhythms as those biological rhythms whose free running period approximates the period of the earth's rotation (that is, approximately 24h). There is practically no physiological, metabolic, or practical outcome in an organism that does not involve/or is not modulated by the circadian clock (Bhadra et al 2017).

1.9.1 Characteristics of the circadian system

Cues about the time of the day or seasonal change are signalled to the body from the external environments via zeitgebers (German for 'time givers'). For example, changes in photoperiod (length of day) can form a zeitgeber. This process of the clock synchronizing itself to the zeitgeber such as light-dark cyclic environment is called entrainment. The relationship between the timing of biological clock and the timing of the external time cue (for example through a Zeitgeber such as light) is called the phase of entrainment. Without a Zeitgeber, the cells in the body display rhythms with periods of about 24 hours.

Specific generalizations about circadian rhythms were proposed by Colin S. Pittendrigh, one of the founding fathers of Chronobiology: circadian rhythms can be understood as those biological rhythms that oscillate for a free running period approximate to the period of the earth's rotation (24 hours). Rhythms can be considered 'free running' rhythms when they slef-sustain and oscillate with a near 24h period during constant light/dark conditions when other environmental zeitgebers are also absent. These self-sustaing rhythms are what justifies the clock as an endogenous mechanism. Circadian rhythms are present in all eukaryotic living systems, and they are self-sustaining oscillations produced by endogenous biological timekeeping mechanisms). The free running rhythm displays remarkable precision; however, this rhythm is not experienced as a fixed characteristic in the organism and is subject to spontaneous and induced shifts within a range (Merrow and Harrington, 2020. The free running period is light intensity dependent and reflects a compensation from temperature variabilities. Both internal and external cues can represent zeitgebers; however light entrains the central circadian pacemaker in the brain, driving daily rhythmic changes in body physiology, and in turn creating cellular zeitgebers such as body temperature, food intake and hormonal output affecting peripheral clocks (Merrow and Harrington , 2020).

In 1971, Konopka & Benzer's work with 3 separate clock gene mutant fruit flies and its resulting change in circadian functions, marked the beginning of the quest for discovering molecular mechanisms governing circadian rhythms (Huang, 2018). The circadian system development occurs postnatally in mammals (Brooks & Canal, 2013). For human infants a cortisol secretion rhythm develops at 8 weeks, melatonin, and sleep efficiency at approximately 9 weeks and rhythmic variations in body temperature and circadian gene expression at 11 weeks (Joseph et al 2015; Yates, 2018).

1.10 The Circadian Clock within our Body- A Well Organised Orchestra

Merrow and Harrington (2020) compared the circadian system to an orchestra, where the 'players', (body's cellular oscillators) follow the conductor (zeitgeber) to reliably communicate its pace according to a specified set of rules. At its core, circadian rhythms are generated through a molecular clock located in nearly every cell of the mammalian body which has an internal timing of about 24 hours even in the absence of external prompts. These clocks located at the peripheral tissues are organised in a hierarchical system, at the top of which is the 'master' clock located in the Suprachiasmatic nucleus (SCN) (a cluster of approximately 20000 neurons in humans (Welsh et al 2010), each generating rhythmic oscillations) nested just dorsal to the optic chiasm in the anterior Hypothalamus of the brain (Takahashi, 2006). Entraining the body to the 24-hour light and dark conditions, this structure takes the role of a caliberator, however this also acts like an endogenous clock. This is because the SCN synchronizes the body to a close to 24 hours free running rhythm even in the absence of bodily rhythms (Gu et al 2021).

1.10.1 The SCN and Light

Light input captured by melanopsin expressing intrinsically photoreceptive retinal ganglion cells (ipRGC) travel through the optic nerve to the SCN and synchronizes the cell's internal clock timing to the external solar day. Endocrine and systemic cues then pass this information to the peripheral clocks across other body tissues (Dibner et al 2010). Output from the SCN regulates physiological processes leading to endocrine rhythms (governing the secretion of cortisol, thyroid stimulating hormones, gonadotropins and melatonin); cardiovascular rhythms (governing the body's blood pressure and heart rate); biophysical rhythms (temperature) and behaviour (including sleep/wake/activity cycles) (Serón-Ferré et al 2001). The SCN comprises of two subregions, the 'core' (which consists vasoactive intestinal

peptide (VIP) and gastrin-releasing peptide (GRP) and the 'shell' (which consists of arginine vasopressin, AVP). The level of VIP (which maintains the clock's internal synchronization) increases during the dark, while increase in levels of GRP occurs during light, activated by input from the retinal photosensitive ganglion cells via the retinohypothalamic tract (RHT) (Hastings et al 2018). The AVP neurons are involved in coordinating the organism's feeding times and thirst control with circadian rhythms. A major efferent projection of the SCN is to the pineal gland, when during night, the neuron fibres release norepinephrine, stimulating postsynaptic adrenergic receptors on pinealocytes, thereby triggering the production of melatonin (which has high lipid and water solubility, allowing it to diffuse easily through the blood brain barrier). Melatonin (N-acetyl-5-methoxytryptamine), which is considered an 'endogenous synchronizer', reinforces various circadian rhythms in the body, by providing night information (Saper et al 2005) (Figure 2, Oishi et a 2021). The intensity of melatonin production depends on the length of night, thereby leading to prolonged production during winter seasons when nights are longer as compared to summer (Sack et al 2007). Melatonin's effect on the brain results from the activation of G protein-coupled receptors, referred to as MT1 and MT2. MT1 receptors are involved in the regulation of rapid eye movement (REM) sleep, whereas MT2 receptors increase non-REM (NREM) sleep (Gobbi & Comai, 2019). In diurnal mammals, nocturnal overexpression of MT2 receptors activate the neurons that trigger NREM sleep, thereby increasing sleep propensity (Brzezinski et al 2005).

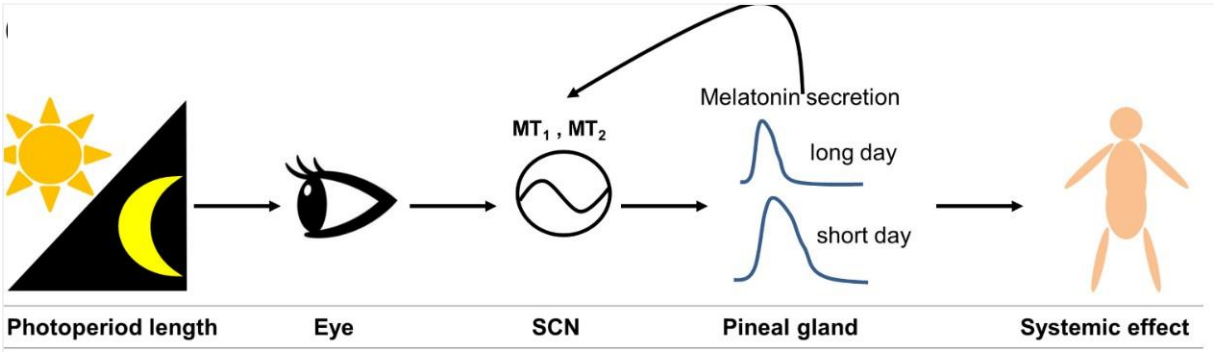

Figure 1.1

Photoperiodic trigger of Melatonin production

Note. Photoperiodic information is received by the retina in the eye, then transmitted through the Retinohypothalamic tract to the SCN which then triggers melatonin production by the pineal gland during the night. In return, melatonin activates melatonin receptors in the SCN and in other central and peripheral tissues. (Diagram and note adapted from Oishi et al 2021).

1.10.2 Peripheral Clocks

Previous literature has demonstrated that the SCN is integral for the generation of circadian rhythms in rodents (Webb et al 2009) and organised intercellular coupling mechanisms allow the neurons to be synchronized to one another. Within the brain, other than the SCN, specific semiautonomous (i.e. olfactory bulb, dorsomedial hypothalamus, arcuate nucleus, habenula) or slave oscillator (i.e. bed nucleus of the stria terminalis, amygdala, preoptic area, paraventricular nucleus, nucleus accumbens) functional nuclei have been noted to have self-sustaining clocks, which are coordinated by the SCN (Fagiani et al 2022).

Circadian clocks outside of the SCN, including peripheral clocks outside of the central nervous system, integrate phase information at the cellular or organ level and influence the time output which results to a clock phase slightly later than the SCN (Mure et al 2018). Ramamoorthy and Cidlowski (2016) explained an example of the above as Glucocorticoid signalling, where SCN triggers a rhythmic release of glucocorticoids from the adrenal glands, through the HPA (hypothalamic-pituitary-adrenal) axis. Glucocorticoid in the blood stream

represents a Zeitgeber that induces clock gene expression and in turn alters oscillations in these cells (Nowak et al. 2021).

1.11 Core Molecular Mechanisms of the Circadian clock

At the molecular level, an autoregulatory transcriptional- translational feedback loop (TTFL) is in operation, responsible for the generation of the approximately 24-hour endogenous rhythms (Mosiek & Holtzman 2016). The following is a snapshot of the core circadian molecular mechanism (Mohawk et al 2012). In this loop (Figure 1.2), the positive transcriptional activator components including the Circadian Locomotor Output Cycles Kaput (CLOCK), Neuronal PAS Domain Protein 2 (NPAS2) and Brain and Muscle ARNT-Like 1 protein (BMAL1) (Dibner et al 2010; Fabiani et al 2022) dimerize and bind with the E-Box elements to initiate the transcription of the Cryptochrome (CRY1, CRY2) and Period (PER1, PER2) genes. The PER and CRY gene products accumulate and form heterodimers to negatively impact the function of the CLOCK:BMAL1 complex in the nucleus, which leads to suppression of its own gene expression. However the cycle is restored as E3 ubiquitin ligase complexes mediate the degradation of the PER and CRY proteins, which consequently leads to the CLOCK: BMAL1 continuing PER and CRY transcription. The CLOCK:BMAL1 & PER:CRY interaction is further regulated via additional feedback loops, prominent among which are the ROR (Retinoic related Orphan Receptors) and REV-ERB (nuclear receptor subfamily 1 group D, NRD1) which are expressed rhythmically due to the binding of the CLOCK:BMAL1 complexes following their interaction with associated E-Box elements. ROR is the positive and REV-ERB is the negative receptor that regulates BMAL1 transcription by binding with the retinoic acid-related orphan receptor response elements (ROREs) (Webb et al 2009). The BMAL-1:REV-ERB:ROR loop fine-tunes the molecular circadian cycle (Hunt et al 2022). The mammalian circadian clock is highly robust and resilient, where only the single-

gene knockout of BMAL1 and double knockouts of CRY1 and CRY2 can result in complete arrhythmicity for the organism in complete darkness (Haque et al 2019; Börding et al 2019).

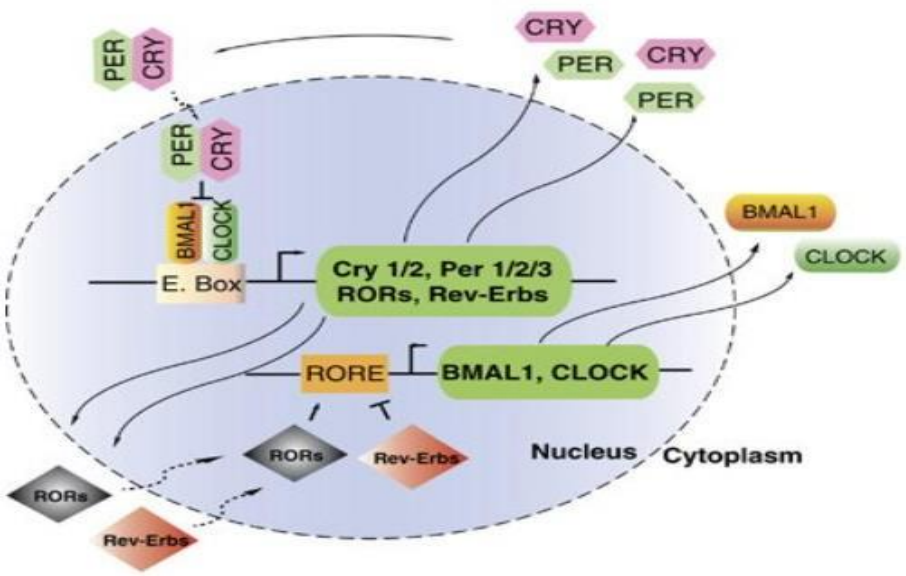

Figure 1.2

Simplified schematic drawing showing the core transcriptional translational feedback loop (TTFL) clockwork mechanism in mammals. (Lee and Kim, 2013).

1.12 The Circadian Clock and its Role in Metabolism

Nowak et al. (2021) explain that there is a bidirectional relationship between the body's circadian rhythm and its metabolism, with the clock controlling every level of metabolic physiology (spanning from cells to the whole organism), and the body's metabolic state influencing the clock (that is the clock in a state of readiness to respond to predictable stimuli, for example food intake). The clock commands the body's metabolic processes through cellular control, organ specific control, neuronal control, and behavioural control (Nowak et al. 2021). Regulation of transcription and metabolite levels (Eckel-Mahan et al. 2012; Nakahata et al. 2009); integration of the nutrient sensors with nutrient receptors with the circadian clock (Zhang et al. 2015; Asher et al. 2008 and Lee and Kim 2013), and mitochondrial respiration

(Schmitt et al. 2018), are some of the pathways through which the clock controls the body's cellular processes (Nowak et al, 2021).

The circadian clock coordinates functions in various tissues or organs via clock-controlled genes (CCGs) (Korencic et al. 2014). For example, the clock plays a crucial role in regulating glucose sensing and insulin secretion in the pancreas, and lack of coordination with the clock can lead to glucose intolerance (Perelis et al. 2015; Sadacca et al. 2011). Adipose tissues store excess energy in the form of triglycerides and regulates their presence in the blood stream. Loss of this regulation due to the lack of a functional clock can lead to obesity and defect in the adipocyte-hypothalamic axis (Paschos et al. 2012). It is known that glucocorticoid hormones, insulin, and appetite controlling hormones play a crucial role in regulating activity and behaviours in organisms (Brown 2016). The HPA axis mediates the secretion of glucocorticoids in response to acute stress, however its secretion also occurs in time of day based rhythmic oscillations (Leviavski et al. 2015). Appetite in humans which peaks in the evening before sleep, as opposed to the morning after an extended fasting period, is also clock controlled (Scheer et al. 2013). Leptin, ghrelin, cholecystokinin and insulin are the major appetite controlling hormones. Adipocytes secrete Leptin that binds to its receptors in the hypothalamus which signals suppression of feeding, whereas leptin resistance and obesity can interfere with the circadian regulation and vice versa (Hsuchou et al. 2013). Ghrelin, which is an appetite stimulation hormone has also been found to display rhythmic oscillations in its secretion (Qian et al. 2019), therefore indicating neuroendocrine-mediated circadian variations in hunger.

1.13 Sleep- A major circadian output

The above discussion shows that the circadian system in living organisms is organized in a hierarchy, with molecular oscillations occurring at the cellular level (including the

transcription-translation feedback loops), and peripheral clocks controlling organ activities in a coordinated rhythm synchronised with the SCN in the brain. The most evident manifestation of this timing system is the sleep-wake cycle, however there are numerous other parameters (ranging from cognitive performance to hormone secretion) where daily rhythms are apparent (Merrow et al. 2005). Sleep can be defined by physiological characteristics in mammals including decreased body movements (as measured through electromyogram), reduced responsiveness to external stimuli, closed eyes, decreased rate of breathing, and altered brain wave architecture (as assessed through polysomnography) (Zeilinski et al. 2016). Whereas human sleep includes apparent ultradian cycles of approximately 90 minutes with 3 stages of Non-Rapid Eye Movement (NREM) sleep and Rapid Eye Movement (REM) sleep, non-mammalian sleep is often assessed by parameters such as periods of decreased motor activity.

1.13. 1 The Two Process Model of Sleep and Wakefulness

Borbely (1982) proposed an the two process model of sleep and wake rhythms in his two-process model of sleep homeostasis. In this model, the sleep/wake cycle is shaped by the interaction of the circadian clock and the sleep homeostat (Borbély et al., 2016). During wakefulness, sleep pressure (S) increases and then dissipates exponentially during sleep (S'). A rhythmic circadian process C, with a near about 24-hour period operating the form of an upper and lower component is the second element of the model. When the rising S intercepts with the upper component of C, and there is a phase of rapid decline, sleep onset occurs (when the upper C component reaches minimum). During sleep, S' decreases exponentially untill it meets the lower component of C, leading to wakefulness (usually after 7 hours), with the cycle then repeating itself. After waking from sleep, cognitive alertness is not immediately evident, a component termed sleep inertia. Investigations have shown that the magnitude of sleep pressure (S) is reflected in heightened subjective fatigue, decreased alertness and the amount

of Slow Wave Sleep (SWS), whereas Slow Wave activity reflects the dissipation of the S' (Doboer , 2018).

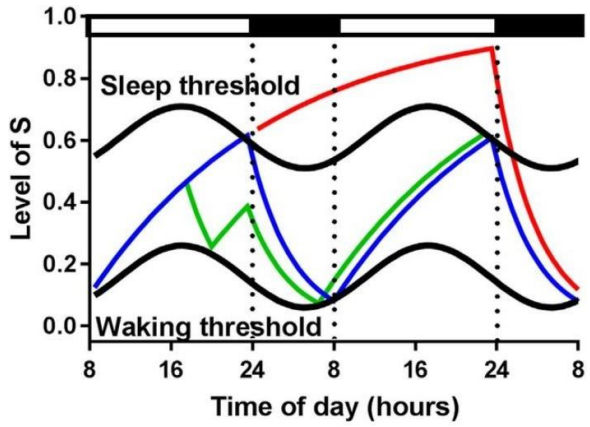

Figure 1.3

*Simplified presentation of the two-process model of sleep regulation (Deboer, 2018).***Note.** *This figure demonstrates the simulation of the homeostatic process S over a two day period, where the sleep-wake periods are demonstrated through the black and white bars, while the blue line is the baseline with 8 hours sleep and 16 hours waking. When the blue line elevates, is the awake period, and when it reaches the top and starts descending, this indicates the sleep period. The green line indicates the effects of a 2-h nap starting around 18:00 followed by normal sleep period at night. The red line indicates sleep deprivation and recovery sleep during the following night. This model assumes that naps and sleep deprivations have no effect on circadian regulation and functioning on the next day. (Adopted fro Deboer, 2018).*

1.13.2 Stages of sleep:

Electroencephalogram (EEG) measurements of brain wave activity is widely used to discern stages of sleep. The neuron's internal membrane properties, neuronal firing and glial activation contribute to the ionic current changes within neurons and the synaptic currents generated by the neuron dendrites form EEG signals (Fields, 2008; Brown et al. 2012; Zeilinski et al. 2016). Sleep occurs in 6 stages of distinct electrophysiological characteristics:

1. Wakefulness or the stage of alertness

This stage is marked by beta waves which are high frequency and low amplitude signals (15-30 Hz). Beta waves are important components of normal consciousness (Engel and Fries,

2010), and they synchronize the activity of spatially distant brain regions. These waves are implicated during heightened alertness, critical reasoning, anxious rumination, concentration and muscle contraction (Zeilinski et al 2016). When eyes are closed and the person is in a state of quiet or relaxed wakefulness (drowsiness), alpha rhythms (9-15 Hz frequency range) are attenuated (Brown et al. 2012). Alpha waves, associated with cognition, are generated through the nerve fibers between the thalamus and the cerebral cortex including the occipital lobe and are regulated through cholinergic inputs from the brainstem (Basar, 2012).

2. NREM sleep stage 1

The first NREM stage of sleep comprises low amplitude mixed frequency electrical activity, with usual muscle tone and breathing rate. This transitional phase of the sleep cycle, usually lasts 1-7 minutes and constitutes 2 to 5 percent of the total sleep time (Carskadon and Dement, 2005; Patel et al. 2022).

3. NREM sleep stage 2

This stage of sleep lasts for about 10-25 minutes and includes low voltage mixed frequency waves. The body in this stage experiences a deeper sleep with lowering body temperature and heart rate, requiring comparatively intense external stimuli to wake up. The presence of sleep spindles and/or K-complexes characterise the electrical activity in this phase of sleep which constitutes about 45 to 55 percent of total sleep time. Sleep spindles, believed to be crucial for synaptic plasticity, result from neuronal firing in the superior temporal gyri, anterior cingulate, insular cortices, and thalamus, inducing calcium influx into cortical pyramidal cells (Patel et al. 2022), whereas K-complexes are 1-second-long delta waves, appearing as the longest of all brain waves. Sleep spindles have been associated with procedural and declarative memory consolidation and learning (Antony et al. 2019; Gais et al. 2002), and

K-complexes have been indicated in maintenance of sleep and memory consolidation (Gandhi et al. 2022).

4. NREM stage 3 and 4 (Slow wave sleep)

This stage of sleep constitutes 25% of the total sleep time and consists of low frequency, high amplitude delta waves. This is the deepest phase of sleep and increase in age is associated with decrease in the quantity of time spent in this stage. The transient phase of sleep inertia is associated with waking from this sleep stage (Hilditch and McHill, 2019). Tissue building and repair, building bone density and muscle and strengthening of the immune system is associated with sleep stage. Sleepwalking, night terrors, and bedwetting occurs during this stage (Shakankiry, 2011).

5. REM sleep

REM sleep, also termed ‘active sleep’ or ‘paradoxical sleep’ constitutes waking like EEG patterns which are coupled with skeletal muscle atonia, except for the active eyes and diaphragmatic breathing muscles (Jones, 2004; Xi et al. 2001). Low-voltage, mixed frequency, ‘sawtooth’ like wave forms consisting of theta (3 to 7 counts per second) and alpha activity are characteristic of REM sleep (Carskadon and Dement, 2005). With regard to neuronal activity, the ventral portion of the sublaterodorsal nucleus of the pons has been implicated, from where spinally-projecting neurons function to produce motor atonia during REM sleep (Lu et al. 2006).

Because new-born mammals spend the majority of their sleep in the REM stage, it is thought to play a crucial role in brain development (Blumberg and Seelke, 2010; Marks et al. 1995). Muscle twitches in REM sleep has been associated with sensorimotor system development, as these twitches occur in a background of muscle atonia, thereby helping the

central nervous system to monitor the origin of each twitch as a result of better signal to noise ratio (Brooks and Preveer, 2016). Studies in rodents and humans have demonstrated that REM sleep facilitates formation and consolidation of spatial and emotional memories (Dumoulin et al 2015; Frank, 2017), although these findings are not consistent across present literature (Siegel, 2001; Horne, 2013; Rasch et al. 2009). Boyce and colleagues (2016), temporally silenced GABA cells that drive theta activity during the REM sleep stage without disturbing the rest of the sleep structure in rodents, which led to erased novel object place recognition and impaired fear-conditioned contextual memory. This validated the memory consolidation functions of REM sleep. In addition, REM sleep selectively crops and maintains synaptic activity related to specific motor learning tasks (Li et al 2017). REM sleep also enables cortical plasticity (Dumoulin et al. 2015; Sterpenich et al. 2014), restoring aminergic cells (Siegel and Rogawski, 1988) and increasing general cognitive creativity (Cai et al. 2009; Wagner and Born, 2001). Dreaming is associated with REM sleep where the loss of muscle tone and motor reflexes prevents the person from acting out their dreams (Bader et al. 2003). Abnormal REM sleep control can lead to neuropathological conditions. These can include REM Sleep Behaviour Disorder, which is characterised by loss of REM sleep paralysis, resulting in sporadic limb movements, shouting, and sometimes punching and kicking (Cygan et al. 2010; Oudiette et al. 2012). Another condition associated with REM sleep is Narcolepsy, which is caused by loss of orexin cells in the hypothalamus, leading to excessive sleepiness, fragmented REM sleep, sleep paralysis, hypnogogic hallucinations (Scammell, 2015) and cataplexy (involuntary skeletal muscle paralysis or weakness during wakefulness) (Dauvilliers et al. 2014).

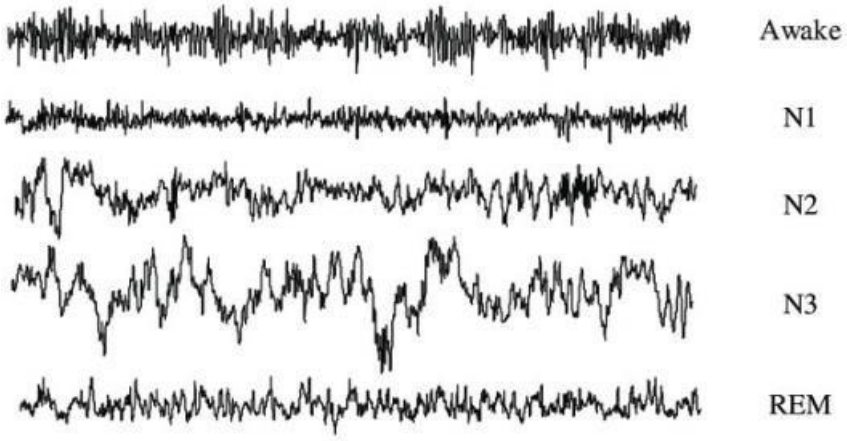

Figure. 1.4

EEG patterns of different sleep stages (Borrowed from Khaligi et al. 2013)

1.13.3 Neurotransmitters involved in promoting sleep and wakefulness

Neurons in the anterior regions of the hypothalamus release GABA (Gamma Amino-butyric Acid) (Gottesman, 2002) which is the main inhibitory neurotransmitter of the brain. GABA inhibits the wake-promoting regions of the hypothalamus and brain stem (Murillo-Rodriguez et al. 2009). Wakefulness promoting neurons located in the basal forebrain, lateral hypothalamus and tuberomammillary nucleus (TMN) are also inhibited by Adenosine (Watson et al. 2010). On the other hand, neurotransmitters such as acetylcholine, dopamine, norepinephrine, serotonin, histamine, and the peptide hypocretin (Orexin) are involved in maintenance of wakefulness (Murillo-Rodriguez et al. 2009). Figures1.4 and 1.5illustrate the wake and sleep promoting pathways.

Regions of the lateral hypothalamus, dorsal raphe nucleus, periaqueductal gray and locus coeruleus (LC) with GABAergic neurons (that uses GABA during its synapse) are activated during NREM sleep (Saper et al. 2010). One NREM network for example involves neurons in the ventrolateral preoptic nucleus (VLPO) of the lateral hypothalamus, that

innervates LC, raphe system, preaqeductal gray, parabrachial gray, and cells in the TMN, thereby inhibiting arousal through these pathways. GABAergic release from melanin containing neurons present in the cerebellum, lateral hypothalamus and zona incerta have been found to regulate NREM and REM sleep. REM sleep includes low amplitude EEG waves, muscle atonia, ponto-geniculo-occipital wave formation (activity in the pons, lateral geniculate nucleus and occipital lobe) and rapid eye movements (Zeilinski et al. 2017). Reciprocal interaction between cholinergic, glutamatergic and monoaminergic nuclei of the brainstem was proposed as a model explaining REM sleep regulation (Hobson et al. 1975); however, almost a decade later GABAergic and the circadian system's influence was incorporated in this model (McCarley and Massaquoi, 1986). The VLPO is also active during REM sleep (Saper et al. 2010). Ventrolateral periaqueductal gray, sub-lateral dorsal nucleus, and lateral pontine tegmentum may regulate the transitions between NREM and REM sleep by inhibiting VLPO neuronal activation.

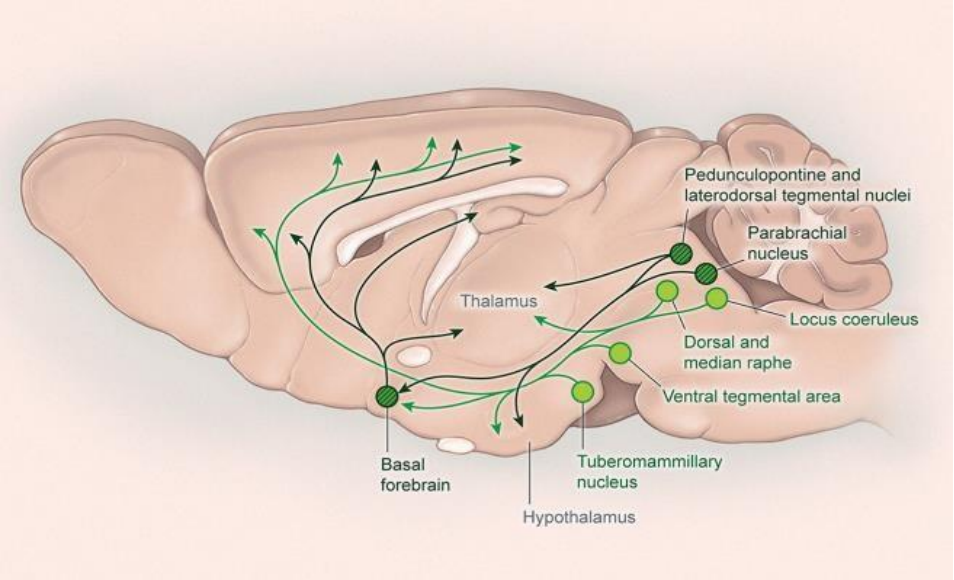

Figure 1.5

Wake Promoting Pathways (Scammell et al. 2017)

Note. Monoaminergic neurons (light green) in the rostral brainstem and caudal hypothalamus directly innervate the cortex as well as many subcortical regions including the hypothalamus and thalamus. These monoaminergic

regions include noradrenergic neurons of the locus coeruleus, serotonergic neurons of the dorsal and median raphe nuclei, dopaminergic neurons of the ventral tegmental area, and histaminergic neurons of the tuberomammillary nucleus. Wake-promoting signals also arise from the parabrachial nucleus and cholinergic regions (dark green with hatching), including the pedunculopontine and laterodorsal tegmental nuclei and basal forebrain. (Figure and description borrowed from Scammell et al. 2017).

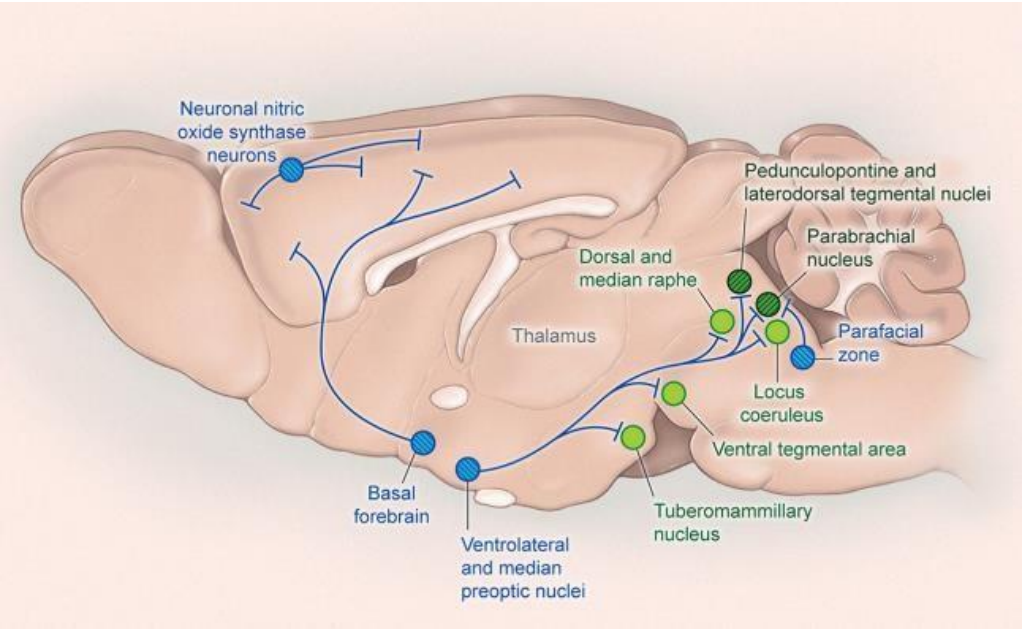

Figure 1.6 *NREM Sleep Promoting Pathways (Scammell et al, 2017)*

Note. NREM Sleep promoting pathways: GABAergic neurons in the ventrolateral preoptic area and median preoptic nucleus promote sleep by inhibiting wake-promoting neurons in the caudal hypothalamus and brainstem. The basal forebrain also contains sleep-active neurons that may promote sleep via projections within the BF and direct projections to the cortex. GABAergic neurons of the parafacial zone may promote sleep by inhibiting the parabrachial nucleus. The cortex contains scattered NREM sleep-active neurons that contain both GABA and neuronal nitric oxide synthase. Blue circles with hatching denote NREM sleep-promoting nuclei. (Figure and description borrowed from Scammell et al. 2017).

1.13.4 A flip-flop switch between sleep and wake periods

Saper et al. (2010) proposed the flip-flop model in which the process of 'mutual inhibition' governs the interaction between the wake promoting and sleep promoting neurons, thereby producing a 'flip-flop' switch in the neuronal electrical circuit. However, it is also important to acknowledge the presence of intermediate states of arousal (for example witnessed in narcolepsy and REM behavior disorder, de Lecea, 2015) and sleep inertia (characterised by impaired cognitive and motor performance after awakening, thought to result from sleep like

patterns in cortical neuronal activity) (Vyazovskiy et al. 2014) where this model might not serve as a useful rationale. As per the flip-flip switch model, REM- switch off GABAergic tegmental and periaqueductal gray neurons inhibit the REM- switch on cells of the parabrachial nucleus (PB) at the junction of the midbrain and pons and the pre-coeruleus. These two nuclei in turn project to the brainstem and spinal inhibitory systems, leading to hyperpolarization of motor neurons and inducing muscle atonia. During REM sleep, VLPO GABAergic REM-on output reciprocally inhibits GABAergic tegmental/periaqueductal grey REM-off neurons (Hobson et al. 1975).

1.14 Developmental changes in sleep patterns among humans

The 24-hour sleep-wake cycle in humans and their associated internal circadian rhythms continuously evolves across the developmental period. Focussing on sleep patterns, during the first 6 months, a human demonstrates most of the waking period during the day and a major nocturnal sleep episode at night (Goons and Guilleminault, 1984), however this pattern changes as development progresses, with a downward trend in frequency and the duration of naps (Seo et al. 2010). Literature has shown a steady decrease in sleep duration, ranging from 12 hours between 2-5 years, 9 hours between 6-12 years, 8 hours in adolescence and 7 hours in adulthood (Galland et al. 2012, Ohayon et al. 2000). A progressively later bedtime during childhood and adolescence is accompanied by a phase delay in the sleep cycle of the individual, which specifically increases with higher age groups (5-7 minutes for children between 7 and 9 years, whereas 10-17 minutes for older children between 9 and 12 years) (Thireifsdottir et al. 2002, Seo et al 2010). Decrease in sleep duration while progressing from childhood to adolescence is ubiquitous to all cultures and countries. Chronotype which is an individual's preference for engaging in activities, is also known to shift towards later in the evening hours as a child grows, which then leads to later bedtimes (Gau and Soong, 2003, Diaz-Morales and

Sorroche, 2008). This shift in chronotype is known to commence at 13 years of age, while reaching to a maximum at the age of 20 for females and about 21 for males (Tonetti et al. 2008, Kim et al. 2002 and Roenneberg et al. 2004) Interestingly, as the developmental age progresses into adulthood and then older adulthood, this shift reverses towards a morning chronotype (Roenneberg et al. 2004, Randler, 2011).

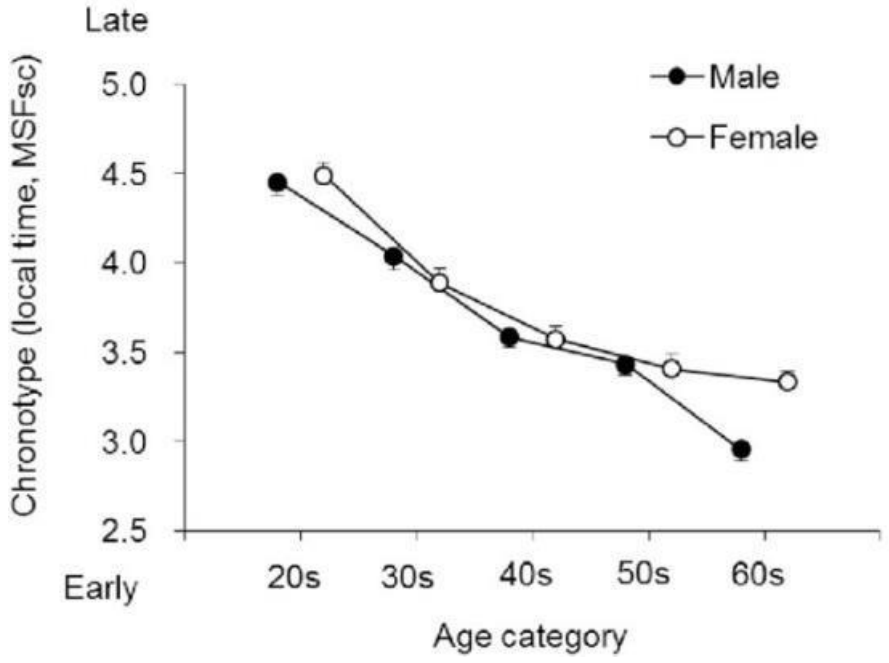

Figure 1.7 *Changes in chronotype with age among males and females. Here, MSFsc is mid sleep on free days corrected for sleep debt. (Figure borrowed from Komada et al 2019).*

1.15 Factors impacting developmental changes in sleep

There are several factors that influence developmental changes in the human sleep wake cycle, including circadian rhythms and neuroendocrine function changes, social demand-based changes in activity schedules and behavioral factors such as physical activity and eating times, or deviation from normal development as a result of delayed sleep phase disorder or mental illness (Carpenter et al.2015).

1.15.1 Changes in Endogenous Circadian Pacemakers

The sleep wake cycle which is designed as per a complex system of endogenous pacemakers, inputs from the environment and molecular feedback loops that result in distinct sequential gene expressions running the clock (Saper, 2013). Endogenous pacemakers include endocrine function and body temperature which undergo developmental changes. For example, the melatonin rhythm is strongest between the age of 4 and 7 and then decreases with continuing development (Attanasio et al. 1985). In the case of cortisol secretion patterns, as the person reaches adolescence, their cortisol level increases and then flattens with pubertal development (Shirtcliffe et al. 2012). Within sleep architecture, while increase in the depth of Slow Wave Sleep is linked with decreasing cortisol level and decreased sympathetic activation, increased autonomic activation and high cortisol activation occur during REM cycles (Steiger 2006). Sex differences in time-of-day cortisol secretion, with a higher level for pubertal girls in the mornings have also been indicated (Keiss et al. 1995, Oskis et al. 2009). Cortisol influences sleep, whereas changes to sleep affect the release of this hormone (van Dalfsen and Markus, 2017).

1.15.2 Body Temperature and Nutrition

Later core body temperature rhythms are associated with evening chronotype for adolescents and adults, whereas the body temperature rhythm phase also shifts to an earlier phase during adulthood (Andrade et al 1992, Carrier et al. 2002). Behavioural factors such as eating and nutrition can also play a role in developmental changes in sleep-wake cycle. Pubertal malnutrition is linked with decrease in sleep duration and longer sleep onset latency (Carskadon et al. 1993). This also links the fact that pubertal hormones influence sleep (Randler et al. 2012), a relationship also demonstrated longitudinally (Sadeh et al. 2009).

1.15.3 Light exposure

Light exposure in terms of increased input in the evening and decreased morning light can delay the phase of the clock (Roenneberg et al. 2003; Goulet et al. 2007), which also might be a reason for developmental change in sleep patterns (Vollmer et al. 2012). Therefore age-related cultural practices (watching TV, using electronic media) and occupational demands (office work in the evening, increased academic demands, vocational tasks) can influence exposure to light, and thereby a shift to eveningness (Cain and Gradisar, 2010, Gamble et al. 2014, Hansen et al. 2005, Short et al. 2011). Age dependent decrease in total sleep time (and resultant daytime sleepiness) among school children may be related to steady pattern of cutting short sleep periods either due to early wake times or increased academic tasks late into the night (Anders et al. 1978, Liu et al. 2008, Ohayon et al. 2004).

When mentioning cutting down on sleep time, the implications of such restriction should be further considered. A considerable body of literature has demonstrated that shorter sleep duration and sleep problems are associated with deteriorated cognitive functions (Kronholm et al 2009; Nebes et al 2009 & Ferrie et al 2011). Interestingly, a short nap post lunch has found to better levels of alertness, short term memory and its accuracy (Waterhouse et al 2007) on the other hand 11 hours or more of night sleep was found to be related to lower total cognitive scores as compared to 7 hours of sleep (Faubel et al 2009). For the above patterns, considering specific changes on the individual's circadian phase affecting cognition might be helpful, for example deteriorated memory and verbal fluency followed by delayed weekend sleep (Yang & Spielman, 2001). As such, there are two types of sleep loss; one continuous wake period Vs chronic sleep loss over a number of days. Van Dongen et al (2003) studied the waking neurobehavioural and sleep physiological effects of chronic sleep restrictions over a period of 14 days in healthy adults, while comparing these measures with 1-2 days of total sleep deprivation. 4 hours and 6 hours of sleep restriction led to deficits in

cognitive functions comparable to 1 to 2 days of complete sleep deprivation, thus demonstrating that when sustained night after night, even moderate sleep restriction can seriously impair neurobehavioural functions. Another interesting observation surfaced where subjective reports of sleepiness ratings did not worsen with increased hours of sleep restriction (i.e. from 4-6 hours to 8 hours) thereby suggesting that once sleep restriction is chronic the individual can not accurately report their sleepiness levels (Van Dongen et al 2003). Therefore, altered patterns of light exposure across the developmental periods might be related to varied restrictions on sleep, the effect of which might not be accurately perceived subjectively leading the person to engage in behaviours solidifying/or enhancing such patterns.

1.15.4 Physical Activity

The magnitude of physical activity a person engages in alters with age, with peaks in mid childhood and a steady decrease along adolescence and an associated increase in sedentary behaviours (Toriano et al. 2008, Arundell et al. 2013, Klinker et al. 2014). Reduced activity and heightened sedentary behaviors in turn are associated with risks of obesity, cardiovascular diseases, diabetes as well as changes in sleep-wake cycles (Gordon-Larsen et al. 2004, Hardy et al. 2009, Edwardson et al. 2012).

1.15.5 Psychopathology

Adverse mental health outcomes are related to changes in sleep-wake cycles. Shortened sleep duration, delayed sleep onset and offset, limb movements, sleep disordered breathing, fragmented or disrupted sleep, nightmares and panic attacks are some deviations from normal sleep found in several neurodevelopmental and mental disorders (Benca et al. 1992, Hasler and

McClung, 2021, Bondopadhyay et al. 2022, Glozier et al. 2014, Papadimitriou et al. 2005, Kessler et al. 2005). Associated symptoms of neurodegenerative disorders, such as Alzheimer's can include not only reduced sleep time, but also changes in sleep architecture such as decreased REM sleep and sleep spindle activity (Fernandez and Luthi, 2020). Prodromal statesof psychiatric disorders as well as more severe symptomatology has also been linked with worse sleep related functional outcomes (Jackson et al. 2003, Young and McGorry, 2006)**.**

1.16 Changes in sleep linked to disorder??

Chronic sleep deprivation is associated with adverse neurocognitive functioning (Hirota and Kay, 2015), emotional and behavioural dysregulation (Yoo et al. 2017) increased sensitivity to pain (Alexandre et al. 2017), weakened immune response, increased risk of cardiovascular and metabolic diseases (Broussard et al., 2012; Huang et al., 2020), neurodegeneration, inflammation, cancer and even death. An individual can deprive themselves of adequate sleep, due to psychological, environmental, and physical factors. Specific populations such as teenagers (Brooks et al. 2015), night shift workers (Reynolds et al. 2022) and elderly populations might have disrupted sleep patterns or reduced sleep duration (Miner and Kryger 2017). For shift workers, misaligned body's internal clock, which is in a sleep state during work, and in sleep during the body's internal day state has been studied (Reynolds et al. 2022). Misaligned light exposure for these workers and its effects, who experience day light while leaving work in the morning after having stayed awake throughout the night in artificial light, for example has been explored (Arendt 2010).

The chronic sleep deprivation alters release of hormones such as cortisol (facilitated by the HPA axis). Sleep deprivation is also linked to regulated synthesis of neurotransmitters, for example, Dopamine, which is in turn associated with a host of psychopathologies (Hasler and

McClung, 2021). The following table iterates the various emotional, cognitive and health related impacts of chronic sleep disruption.

Table 1.2

The impact of chronic sleep and circadian rhythm disruption upon human health (borrowed from Foster, 2020).

Emotional	**Cognitive**	**Physiology and health**
increased	impaired	Increased risk for
fluctuations in mood	cognitive performance	daytime sleepiness
irritability	ability to multi-task	micro-sleep
anxiety	memory	cardiovascular disease
loss of empathy	attention	altered stress response
frustration	concentration	altered sensory threshold
risk-taking and impulsivity	communication	infection, lowered immunity
negative salience	decision-making	cancer
stimulant use	creativity and productivity	metabolic abnormalities
sedative use	motor performance	diabetes II
illegal drug use	dissociation	depression and psychosis

Disorders associated with sleep itself might affect sleep architecture and patterns (with usual onset in childhood or adolescence) or example in the case of delayed sleep phase disorder (delayed onset and offset of sleep timing) (Thorpy et al. 1988, Crowley et al. 2007). Sleep disorders are characterised by disruption in normal sleep pattern or sleep behaviours. The major conditions in this category includes insomnia, hypersomnia, obstructive sleep apnea and various parasomnias.

1.17 Disorders of sleep

Insomnia is associated with difficulty getting to sleep, high sleep onset latency or maintaining sleep, with associated psychological, physiological and functional consequences (Worley, 2018). Difficulty getting to sleep is significant problem even in the general population, with 20-30% having poor sleep, 8-10% suffering from chronic insomnia, and 4% taking sleeping pills (Bixler et al. 2002, Ohayon, 2002 and Chong et al. 2013). Insomnia is associated with the presence of adverse cardiometabolic outcomes such as hypertension, type 2 diabetes and even risk of acute myocardial infarction (Suka et al. 2003, Laugsand et al. 2011, Kawakami et al. 2004). The psychological clinical picture of a person with insomnia includes cognitive and emotional hyperarousal characterised by obsessive thoughts, anxiety, ruminative tendencies, dysthymic personality traits and emotional oriented coping strategies (Kales and Kales, 1984, Leblanc et al. 2007, Morin et al. 2003). In addition to the above, impairments in cognitive functioning in the form of attention, concentration and memory problems have also been indicated in insomnia (Riedel and Lichstein, 2000).

Sleep-related breathing disorder (SRBD) include conditions such as obstructive sleep apnoea (OSAS) (blocking of the breathing mechanism due to obstruction to the upper airway), central sleep apnoea syndrome (CSAS) (cessation of breathing due to absent respiratory effort), and hypoventilation disorders (shallow breathing caused by other medical conditions) (Worley, 2018). The prevalence of these conditions lies at 20-30 % for males and 10-15% for females (Young et al. 2009). Diagnosis of these conditions have primarily been through polysomnography, where overnight simultaneous measures of electroencephalogram, electrooculogram, electromyogram, air flow through mouth and nose, pulse oximetry to assess the level of oxyhaemoglobin saturation are included (not an exhaustive account) (Jaffe et al. 2006). Apnoeas are a 70% or greater decrease in airflow as compared the one in the previous breath, that lasts more than 10 seconds (hypopnea includes 30-70 decrement in airflow) and

can either be obstructive or central in origin. In case of obstructive apneoa, some respiratory effort is seen in the chest excursion while breathing, whereas, for central apneoa, no respiratory action is seen in the chest excursion. (Jaffe et al. 2006). Previous literature has consistently linked SRBD with heightened cardiovascular morbidity and mortality (Marin et al. 2005, Peppard et al. 2000, Shahar et al. 2001). The most demonstrated risk factors for SRBD include obesity, gender (9% in men, to 5% in women), age, and oropharyngeal anatomy (Young et al. 1993, Ancoli-Isreal et al. 1991). Psychiatric comorbidity such as presence of affective disorders, schizophrenia, anxiety-mood traits (Milman et al. 1989, Mosko et al. 1989, Ohayon, 2003, Aikens et al. 1999).

Disorders of hypersomnolence include excessive daytime sleepiness which cannot be attributed to other sleep disorders (Worley, 2018). Central disorders of hypersomnolence include, Narcolepsy type 1 (with cataplexy), narcolepsy type 2 (without cataplexy), idiopathic hypersomnia, Klein- Levine syndrome, hypersomnia due to medical disorder, substance use or medication, psychiatric disorder and insufficient sleep syndrome (American Academy of Sleep Medicine, 2014). Narcolepsy is characterised by excessive daytime sleepiness, cataplexy, sleep paralysis and hypnopompic or hypnogogic hallucinations (Khan and Trotti, 2015). Cataplexy, which is present in 65% to 75% of individuals with narcolepsy is defined as a sudden loss of muscle tone which occurs in response to a strong emotion (usually humorous) (Silber et al. 2002, Guilleminault et al. 1994). Cataplexy can be understood as an inability to maintain state control, for example a feature like REM sleep suddenly occurs during complete wakefulness (Saper et al. 2005). Prevalent pharmacotherapeutic treatments for hypersomnia include compounds such as modafinil, or central nervous system stimulants, whereas for narcolepsy type 1 sodium oxybate is effective (Khan and Trotti, 2015).

Circadian rhythm sleep–wake disorders are associated with deviations from normal sleep–wake cycles caused due to a misaligned biological clock and the individual's required sleep wake times. Conditions in this category of sleep problems include delayed or advanced sleep phase (Delayed sleep phase syndrome (DSPS) or Advanced sleep phase syndrome (ASPS) respectively), shift work disorder, and jet lag (Worley, 2018). These disorders can be attributed to both internal and external factors. Internal factors include phase shifts to advanced or delayed sleep times (delayed sleep phase disorder, advanced sleep phase disorder, irregular sleep wake rhythm, and free-running disorder), which may also be demonstrated in patients with neurodegenerative disorders (such as Alzheimer's and Parkinson disease), head trauma or encephalitis. External factors like jet lag and shift work can put body rhythms of temperature and hormone secretion out of sync with the light dark cycle (Schwab, 2022). This desynchronization may be associated with nausea, lethargy, irritable mood, depressogenic cognitions as well as risk of cardiovascular and metabolic disorders. 0.17% of the general population might have DSPS, whereas 7-16% adolescents might have this syndrome (Regestein and Monk, 1995). A detailed history, comprehensive report of the patient's sleep wake patterns through sleep diary, actigraphy and examining circadian rhythm markers such as core body temperature and melatonin are useful means of diagnosing this condition (Zhu and Zee, 2012). Etiological factors for these conditions can include genetic vulnerabilities, physiological, environmental mechanisms. For example, an extraordinarily long endogenous circadian period may alter the relationship between sleep onset and offset (Ozaki et al. 1988), hypersensitivity to melatonin suppression at night (Aoki et al. 2001), altered homeostatic process as shown through alterations in slow wave activity (Watanabe et al. 2003), light history exposure can be some of the causes. The management of sleep wake disorders involves a combination of need based therapeutic modalities, such as behavioural guidance, structured physical activity, light exposure, minimizing night light and noise exposure and use of

pharmacological agents such as melatonin, modafinil, armodafinil, stimulants (Zhu and Zee, 2012).

Parasomnias would be a category of sleep disorders involving abnormal behaviors or events arising during the sleep event, including sleepwalking, sleep terrors, and rapid eye-movement sleep behavior disorder (Worley, 2018). Sleep-related movement disorders involve recurring movements in sleep, such as restless legs syndrome, periodic limb movement in sleep and leg cramps (Worley, 2018).

1.18 Sleep in different psychiatric disorders

Among the functional difficulties associated with psychiatric disorders, those which are common, are often downgraded in their importance and overlooked, both in research and clinical practice. Mental health conditions are often presented not as unitary set of signs/symptoms, but as a dynamic interconnected network of presentations (Contreras et al. 2019). One of these dynamic signs, present in different natures are chronic sleep problems for the individual. Research has focussed on how these sleep problems might be a contributary factor in the disorder and how they differ in their presentations with differing levels of severity/ differences in the clinical presentation of the symptoms (Paterson et al, 2013; Roberts and Duong, 2014). For some disorders, difficulty initiating sleep or insomnia related problems are often common and can also form a bidirectional relationship with the disorder in question (Mulraney et al. 2016).

The magnitude and quality of sleep can influence the optimal functioning of the brain (Eugene and Masaik, 2015; Tai et al. 2022). Neurocognitive functions such as alertness, behavioural/emotional/cognitive regulation, memory formation, executive functions, as well as hormone regulation and various aspects of behaviour are affected by sleep (Devore et al.

2014; Kronholm et al. 2009; Krause et al. 2017; Kim et al. 2015). Structured experimental sleep deprivation among healthy participants have resulted in varied forms of impairment. These range from psychopathological (Kahn-Greene et al. 2007), to lowering of physical agility/motor functions (REF), to memory deficits (Van der Helm et al. 2010).

Alterations in neurotransmitter circadian patterns have been linked to altered sleep wake patterns in individuals as seen in some psychiatric disorders. For example release of the wake promoting neurotransmitter orexin, may lead to insomnia/hypersomnia in affective disorders (Nollet and Leman et al 2013). On the other hand narcolepsy, which is often accompanied by major depression and anxiety disorders (Ohayon et al. 2012) is also caused due to orexin deficiency (Mahoney et al. 2019). However, these associations can also be attributed to genetic links between sleep and behaviours (for example, clock gene polymorphisms was found to be associated with affective conditions (Partonen, 2012; McClung, 2007). Studies involving orexin receptor antagonist has continuously been conducted on animal models for their possible therapeutic effects (for anxiety, compulsive traits, eating concerns and additction to substances) Merlo and Melotto, 2014). In such conditions (for example in ADHD, Hiscock et al 2015) or depression, Manber et al. 2008) research is attempting to create the base for evidence-based sleep interventions.

1.18.1 Sleep in Depression

Before discussing the topic of sleep in depression it is perhaps useful to recall that within major clinical features, inability to fall asleep or sleeping too much is a key sign of depression. Although majority of patients with depression report sleep disturbances, and some of these concerns subside with alleviation of the depressive symptoms, however for some individuals these might continue and increase the risk of relapse (Jindal and Thase, 2004). A bidirectional association can be stated between depressive symptoms and sleep issues, making

it yet another complex riddle to unravel (Frazen and Buysee, 2008). Incidence of insomnia (75%), hypersomnia (15%) and obstructive sleep apnoea (20%) has been indicated in this condition (Nutt et al. 2008). Ağargün et al (1997), found that while both insomnia and hypersomnia are associated with suicidal ideations and attempts, insomnia also significantly predicts depressive symptoms. A large sample (n = 24,686) survey revealed that less than 6 and more than 8 hours sleep duration was associated with features of depression and that lower subjective sleep efficiency was related to higher depressive symptoms (Kaneita et al. 2006). Disturbed sleep is reported by parents in childhood populations both for typically functioning and those diagnosed with depressive disorders mainly through subjective measures such as parent-teacher questionnaires or interviews (Gregory and O'Connor, 2002; Lovato et al. 2017). Prevalence of sleep difficulties within this clinical population is higher for girls (Barclay et al. 2015).

1.18.2 Sleep in Anxiety Disorders

Anxiety as a psychological experience can be understood as one of the responses to stress. Anxiety encompasses systematic activation of two systems of the body: the corticotropin-releasing hormone (CRH) system and the autonomic nervous (AN) system, that help to regulate arousal responses with the aim of maintaining the central nervous system in a state of survival (Sukhareva, 2021).

The arousal responses can be hormonal, behavioural or autonomic in nature based on the nature of stress perceived by the organism, for example, in case of a physiological stress the AN system gets activated, while in case of complex environmental situations such as a unpleasant emotions the CRH system is activated. Both animal and human studies have demonstrated the effects of acute or chronic stress on sleep (Gonzales and Valatx, 1997; Cheeta et al. 1997; Marinesco et al. 1999). In response to stress the CRH initiates activation of the

Hypothalamus- Pituitary- Adrenal (HPA) Axis, which in turn regulates the metabolic, immune responses and the autonomic nervous system, through a complex set of positive and negative feedback mechanisms occurring between the hypothalamus, pituitary gland and the adrenal gland. During slow wave sleep (SWS) the HPA axis is in a state of pronounced inhibition, whereas during before wake REM sleep it reaches its diurnal maximum strength. Within the general population, the association of sleep disturbances with anxiety has been consistently demonstrated (Breslau et al. 1996; Ford and Camerow, 1989; Ohayon and Roth, 2003), whereas lifetime sleep disturbances have significantly predicted anxiety disorders such as obsessive compulsive disorder (OCD), panic disorder and generalised anxiety disorder (GAD) (Breslau et al. 1996).

In addition to the apprehensive 'worry' that disrupts the quality of sleep, there might be concerns in sleep caused by motor tension (muscle tension, sense of restlessness and fatigability) and those caused by hypervigilance associated with anxious cognitions (difficulty relaxing and winding down to sleep causing increased sleep onset latency, disrupted sleep, difficulty continuing in the relaxed state and irritability) (Staner, 2022). 18% patients with panic disorder can experience nocturnal panic attacks (Taylor et al 1986), although sleep related panic is most reported within this population (Mellman and Uhde, 1990). Differentiating nocturnal panic attacks from sleep apnoea, night terrors , nocturnal epilepsy or night time arousal is crucial for the most appropriate treatment (Craske and Rowe, 1997). Objective investigations, such as nocturnal polysomnography, have not been able to present a clear picture regarding alterations in sleep architecture in anxiety disorder although these gaps could be attributed to illness severity, comorbidity or developmental age of the sample (Staner, 2022). Especially because anxiety is part of the clinical picture of a host of other psychiatric conditions, differentiating it and establishing its relation with sleep is a complex task.

1.18.3 Sleep in Neurodegenerative Disorders

Circadian and sleep dysfunctions have been consistently demonstrated across literature in neurodegenerative disorders such as Alzheimer's (AD), Parkinson's (PD) and Huntington's (HD) disease (Fifel and Videnovic, 2021). Overt behavioural circadian disturbances such as altered sleep- wake behaviours (for example, frequent day time naps, changes in phase angles, rest/activity fragmentation and reduced sleep wave amplitudes) have been reported in these conditions (Ortiz-Tudela et al. 2014; Hooghiemstra et al 2015; Wang et al 2015; Weissova et al 2016), and typically occur before the main clinical characteristic of the disorder itself (Saper, et al 2005). Other functional alterations for circadian markers have been found in AD, PD and HD, such as modified circadian amplitude of cortisol rhythms (Adamczak-Ratajczak et al. 2017), amplitude disruption of melatonin secretion cycles (Fifel, 2017), loss of the diurnal rhythm in blood pressure and heart rate variability (Baschieri and Cortelli, 2019), reversal of urine excretion patterns (Ouslander et al. 1998) and alterations in body temperature (Raupach et al. 2019).

Sleep problems in AD exist within a bidirectional relationship with the condition's characteristics (Wang and Holtzman, 2020). While pathogenesis of AD is linked with accumulation of amyloid- β (Aβ) peptide in the brain, sleep deprivation is also related to increases in soluble Aβ and, while patients with normal cognitive functions and early Aβ deposition have deviant sleep functions, this is also the case for individuals who have mild dementia due to AD (Ju et al 2014). Sleep difficulties manifest in the form of fragmented sleep, with shorter duration sleep episodes, excessive sleepiness and diurnal psycho-behavioural changes as the evening sets, which in turn causes functional difficulties for caregivers (Terum et al. 2017). For PD, in addition to disrupted night-time sleep, primary sleep disorders such as REM sleep behaviour disorder (Sixel-Doring et al. 2016) and restless leg syndrome are reported (You et al 2019). In Huntington's disease (characterized by deficits in motor

movements, cognitive deterioration, and psychiatric comorbidities), is associated with alterations in sleep architecture, such as reduced N3 stage and increase sleep spindle activity (Wiegand et al 1991), as well as reduction in total REM sleep time (Hansotia et al. 1985). RBD has also been associated with HD (Videnovic et al. 2009). Although sleep research in neurodegenerative disorders is still at a young stage, sleep and circadian disturbances have been reported both as causes and consequences of these conditions (Fifel and videnovic, 2021)

1.18.4 Sleep in Autism

40% to 80% of children and young persons diagnosed with Autism Spectrum Disorder (ASD) present sleep problems, in particular insomnia (Cortesi et al, 2010), with associated concerns in frequent awakenings, early morning awakenings, bedtime resistance, parasomnias, sleep disordered breathing and daytime sleepiness (Krakowiak et al. 2010; Taira et al. 2008). The causal factors involved for sleep problems is ASD are multifactorial, with neurological, genetic, and environmental aspects requiring attention. Previous literature has indicated that the neurotransmitters, GABA, serotonin, and melatonin play an important role in regulating the sleep wake cycle (Cortesi et al, 2010). For example Melatonin regulated the body's circadian clock, and this neurotransmitter has shown abnormal synthesis in ASD, while treatment with melatonin has shown improved sleep patterns (Leu et al. 2011). Also the major sleep promoting areas of the hypothalamus use GABA, which also had less matured interneuron migration among ASD individuals (McCauley et al. 2004).

Regarding alterations in sleep architecture in this population, PSG studies have shown decreased overall sleep quantity, alteration in eye movement organisation, reduced total sleep and bedtime, REM sleep time and increased proportion of stage 1 of NREM sleep (Elia et al. 2000; Malow et al 2006). Regarding consequences of the above discussed sleep difficulties, there effects are significantly felt and have been consistently reported by caregivers. In addition

to maternal or parental stress, these sleep difficulties also effect the quality of life of the child and their overall functioning (both practical day to day tasks and emotional regulation) (Devnani and Hegde, 2015). Currently research in this topic involves either or the combination of both subjective (questionnaires, surveys and interview) and objective measures, including polysomnography and actigraphy methods (18, 19). Devnani and Hegde (2015) propose that sleep queries in should be elicited in the form of a systematic sleep history format including predisposing, precipitating, and perpetuating factors. In case of possible sleep promoting steps, caregivers are directed towards the child's environmental (making the environment more comfortable by acknowledging the child's sensory needs such as, temperature, bedding and clothes), bedtime routine (visual bedtime schedule, reminders and consistency) and sleep training aspects.

1.19 Sleep in ADHD

Children diagnosed with ADHD often have disturbed lifestyles, with a host of disorganised behaviours constantly tinting their daily lives. Although these behaviours may be goal directed, they frequently end up being incomplete or filled with errors, resulting in detrimental implications for their mental health and occupational endeavours. Within the facets of their disturbed lifestyle, individuals with ADHD often report experiencing sleep related concerns and disturbances in considerable excess compared to matched control groups (Owens 2009). Co-occurrence of sleep concerns and ADHD reflect their prevalence in a pronounced way, with 70% of individuals with ADHD having sleep related concerns (Yoon et al. 2012) as opposed to 20–30% in the general population (Quach et al. 2012). Such sleep related concerns reported include sleep onset problems manifesting in long sleep latency, sleep phase delay syndrome, increased periodic limb movements during sleep, daytime sleepiness and altered total sleep (Corkum et al. 1998; Cortese et al. 2006; Konofal et al. 2001, 2010; Mayes et al.

2009). A number of the above concerns are expressed as difficulty in initiating and maintaining sleep (Ball et al. 1997) and the severity of sleep problems may be associated with the severity of ADHD symptoms and may be useful therapeutic targets for ADHD symptom management (Sciberras et al. 2019). Further, in the general population sleep disturbances may be associated with inattention and hyperactivity; for example, Sung et al. (2008) demonstrated that children with behavioural sleep problems also experienced more ADHD-like symptoms, lower quality of life and daily functioning. As such, dysfunctional behavioural traits associated with ADHD might be related to impaired sleep functioning, which in turn acts as a maintaining factor for the condition, fueling the core characteristic features of the disorder (Coogan et al. 2016a). However, looking from the perspective of primary sleep disorders as well (Schutte-Rodin et al 2008), the effect of chronic insomnia on daytime activities and functions including those of mental inefficiency, difficulty remembering, difficulty focusing attention and completing mental tasks are apparent. Indeed, some authors have recently questioned whether ADHD should be considered primarilyas a sleep disorder (Bijlenga et al. 2019). However, there are a number of central questions that remain unanswered in relation to the sleep-ADHD associations, including questions of causality, directionality and mechanism (Raman and Coogan 2019).

Looking at the lifespan perspective, as mentioned earlier age-related changes in sleep have been well researched and validated. Especially looking at the time of adolescence and pre-adolescence, this is a time of speedy neurobiological, psychological, and socio-cultural changes, that have the potential to impact sleep (Crowley et al 2018), ever so for the ADHD population (Becker 2020). Becker et al 2019 found that among 8th grade adolescents, those with ADHD were more likely to get poor sleep on school days (indicated both by sleep diary and actigraphy), when compared to the neurotypical control group. When underlying the attributional factors for the above, the role of excessive nighttime social media use, general preoccupation with screen based technology, lack of sleep hygiene and routines, coupled with

academic demands can be mentioned (Becker et al 2018; Bourchtein et al 2019; Martin et al 2018). Especially for the ADHD population, along with the above factors, the role of comorbid psychopathologies, ADHD related emotional- behavioral dysregulation and family/peer related interpersonal difficulties could be highlighted (Becker 2020). Although sleep related problems have also consistently been reported in adults with ADHD (Coogan and McGowan, 2017), examining sleep in early years of development (i.e., amidst childhood presentation of ADHD) would help capture its negative consequences on ADHD features/severity, comorbid psychiatric factors and physical health. Within the investigations in this thesis, we have therefore focused on the childhood years primarily.

1.20 The Circadian System and ADHD

Both objective and subjective assessment tools examining the rest and activity cycles among individuals with ADHD (children, adolescents and adults) have shown significant variations in daily rhythms in a number of behavioural, cognitive, endocrine, physiological and molecular parameters when compared to typically functioning individuals (Korman et al. 2019). An important behavioural and psychological manifestation of variations in circadian functioning is chronotype/diurnal preference (Adan et al. 2012). Chronotype/diurnal preference can be broadly conceptualised as inter-individual differences in actual or preferred timing of sleep/ wake behaviours, and psychometric and other instruments such as the Morningness/Eveningness Questionnaire (Horne and Ostberg 1976), the Composite Scale of Morningness (CSM, Smith et al. 1989) and the Munich ChronoType Questionnaire (MCTQ,

Roenneberg et al. 2003) can be used for its assessment. Both children and adults with ADHD have been found to have a significant preference for eveningness/later chronotype, characterised as later bedtime and wake time or an increased psychological preference for such later timings of sleep behaviours (Baird et al. 2012; Durmus et al. 2017; Rybak et al. 2007; Voinescu et al. 2012). These preferences are also related to greater severity of ADHD symptoms (Gamble et al. 2013 & Rybak et al. 2007). Some studies have linked later and more variable sleep timing with trait impulsivity (McGowan and Coogan 2018), and have also linked later chronotype with other behavioural manifestations of impulsivity, including sensation seeking and response inhibition (Kang et al. 2015). Ottoni et al. (2012) report that eveningness is associated with being emotionally volatile and the behavioural traits of ADHD such as apathetic and disinhibited temperamental inclinations. Therefore, there may be widespread influence of the circadian system on the individual's cognitive, affective, behavioural domains that are pertinent for ADHD symptomatology.

1.21 Delayed Sleep Phase and Sleep Onset Insomnia in ADHD

The pineal hormone melatonin's synthesis in the pinealocytes from the precursor tryptophan exhibits a clear circadian rhythm, with peak plasma levels usually between 2 and 3 am, and the master pacemaker in the suprachiasmatic nucleus (SCN, located in the anterior ventral hypothalamus) has indirect efferent projections to the pineal gland crucial for synchronising the circadian rhythm of melatonin to the light-dark cycle and maintaining its persistence (Arendt 2005a). Van der Heijden et al. (2005) reported that the presence of sleep onset insomnia in children with ADHD is associated with significantly longer sleep latencies and delayed dim-light melatonin onset (DLMO) compared to children with ADHD but no sleep onset insomnia. Van Veen et al. (2010) found that, out of 40 ADHD adults, 31 reported the presence of sleep onset insomnia and were also found to have a delayed DLMO, indicated a significantly delayed phase of circadian entrainment. In a large retrospective cohort of 9,338

adolescents, a significant association was found between delayed sleep phase disorder (DSPD) and inattentive and hyperactive symptoms (Sivertsen et al. 2015), indicating potential for delayed sleep phase to feed into ADHD symptoms. As such, delays in DLMO observed in ADHD may be indicative of altered entrainment of the SCN master clock to environmental zeitgebers. However, to date there has been no direct examination of SCN function in ADHD (for example, in post-mortem tissue), and other work to date has focussed on the use of peripheral (and accessible) circadian oscillators as proxies for circadian function in ADHD (e.g., Baird et al. 2012; Coogan et al. 2019).

Psychopharmacological factors might also influence the presence of longer sleep latency and other insomnia symptoms sleep in ADHD. In a study by Boonstra et al. (2007), administration of methylphenidate (MPH, the frontline psychostimulant used in the pharmacological management of ADHD) in adults diagnosed with ADHD has been linked to sleep latency and sleep duration. However, the same study also documented evidence of lesser nocturnal awakenings and hence a more consolidated sleep because of MPH (Boonstra et al. 2007). Among the younger ADHD populations, methylphenidate has been linked to a shorter total sleep time and later sleep onset times in several investigations (Lee et al. 2012; Sangal et al. 2006; Snitselaar et al. 2013; Tirosh et al. 1993). Another recent study demonstrated that pharmacotherapy of ADHD was associated with alterations in circadian and sleep function in adults with ADHD when compared to treatment naïve ADHD patients (Coogan et al. 2019). For example, treatment was associated with longer, but not more frequent, wake bouts during the night in medicated patients. As such, it is important to delineate the associations of ADHD itself with sleep and circadian changes arising from ADHD treatment effects.

1.22 Genetic and Environmental Factors linking ADHD and the Circadian System

Similar to ADHD, circadian traits are also reported to be heritable; for example, chronotype appears to be strongly heritable (Inderkum and Tarokh 2018) and genome-wide studies have revealed significant associations with polymorphisms in clock genes and other loci (e.g., Jones and Jane 2019). As such, there is the possibility for shared genetic risk between ADHD and circadian traits associated with ADHD (Demontis et al. 2019; Gregory et al. 2017). Genetic relationship between sleep and ADHD has also been investigated by examining polygenic liability scores for sleep phenotypes to demystify the association between ADHD and sleep problems (Akingbuwa et al. 2020, Takahashi et al. 2020). With regards to clock gene associations, PER1 has been associated with ADHD in children and adolescents (Lasky-Su et al. 2008) and PER2 polymorphisms has also been associated with ADHD (Brookes et al. 2006), although these associations did not reach genome-wide statistical significance. A single nucleotide polymorphism in the CLOCK gene has been associated with adult ADHD symptoms in three separate studies (Jeong et al. 2014; Kissling et al. 2008; Xu et al). Carpena et al. (2019) explored the association between ADHD and CLOCK, using haplotype analysis, and demonstrated an association between CLOCK haplotype and ADHD status, further implicating CLOCK in the aetiology of ADHD. There have also been a number of studies that examined the diurnal rhythms in expression of clock genes in different tissues derived from ADHD patients. Baird et al. (2012) reported that, in adults, ADHD is associated with blunting of rhythms in the expression profiles of the clock genes BMAL1 and PER2. Coogan et al. (2019) also reported ADHD-related changes in clock gene expression profiles in ex-vivo cultures of fibroblasts derived from patients with ADHD (and with or without ADHD medication). These data indicate that there may be alterations in the core molecular circadian cycle associated with ADHD and warrants further study.

As light is the most important environmental zeitgeber that determines circadian phase, it is possible that geographical variations in the timing and levels of exposure to sunlight might influence ADHD prevalence. Arns et al. (2013) tested this hypothesis when they analysed the record of solar intensity from ten countries, reporting associations between higher solar intensities and lower ADHD prevalence. The proposed mechanism that may underpin this association is that bright morning light would phase advance the circadian clock and decrease the association between delayed phase and ADHD symptoms. In 2015, Huber and his co-workers stated that higher altitude geographical regions have lower prevalence of ADHD, based their rationale on the association of higher altitude with hypobaric hypoxia and hence increased levels of dopamine. Based on the hypodopaminergic model of ADHD, such an increase in the dopamine would mitigate against ADHD. However, Arns et al. (2015) found that the association of altitude with ADHD prevalence is actually related to the solar intensity levels rather than the altitude level, which must have been the confounding factor detected previously. The influence of natural sunlight, mediated through the biological clock, on ADHD symptoms may offer therapeutic opportunities through increasing exposure to daylight.

1.23 Circadian Aspects of ADHD specific Neuroendocrine and Autonomic Aspects

Turner-Cobb (2005) showed that the hypothalamus pituitary adrenal (HPA) axis plays an important role in regulating neurobehavioural domains such as attention, emotion, learning, memory and movement. Under a stressful condition, the neurons of the hypothalamus release the corticotropic hormone which in turn leads to the secretion of the adrenocorticotropic hormone and the subsequent secretion and release of cortisol from the adrenal cortex. In a study by Musser in 2011 it was found that there were no significant sympathetic variations found in ADHD children when they were shown emotional stimuli as opposed to typically functioning individuals, supporting the hypothesis of autonomic dysregulation in individuals with ADHD. This under-reactivity of the HPA was also found to correlate with the neurocognitive

performance of the ADHD individual and was further demonstrated empirically by measuring low levels of cortisol for ADHD patients as compared to the control group in a study by Ma and colleagues in 2011. Abnormal diurnal cortisol rhythms have been linked with hyperactivity manifested in childhood features of ADHD (Blomqvist et al. 2007; Kaneko et al. 1993) and this finding is crucial as the HPA axis is under strong circadian control (Nicolaides et al. 2014).

Further, the diurnal profile of cortisol expressed relative to habitual wake time appears to be phase-delayed in adults with ADHD compared to controls (Baird et al. 2012), whilst children with ADHD show morning hypo-arousal of the HPA axis as assessed via salivary cortisol levels (Imeraj et al. 2012). Dysfunction in arousal mechanisms can be viewed as the causal factor for ADHD, with motor hyperactivity being considered a reaction to the hypo-arousal condition that is required to counteract somnolence (Lecendreux et al. 2000). Hence, hypo-reactivity of the HPA axis in stressful condition has been linked to the symptoms of hyperactivity and impulsivity in ADHD (Blomqvist et al. 2007; Hong et al. 2003; Moss et al. 1995; Virkkunen 1985). This behavioural hyperactivity and impulsiveness is expressed in the form of a significant lack of behavioural inhibition characterising their psychosocial reactions. Hong et al. (2003) postulated therefore that an abnormal HPA-axis response to stress should be considered as an attributional factor for the dysfunctional behavioural inhibition observed in ADHD. A corollary of this hypothesis is that given the HPA operates under strong circadian influence, that dysfunction of HPA function in ADHD may be associated with altered rhythms in HPA processes.

The possible dysfunction of the HPA axis has been linked to the major defining characteristics found in ADHD which are cognitive, affective and behavioural in nature. Low levels of cortisol has been associated with lack of age appropriate cognitive performance (Hong et al. 2003), maladaptive behaviours as well as variations in levels of anxiety among ADHD

children (Hastings et al. 2009); these findings have also been replicated in adults with ADHD (Lackschewitz et al. 2008). Certain studies have shed light upon specific relationship between the ADHD subtype and under-reactivity of HPA axis in response to stress. Both hyperactivity/impulsive subtype and the inattentive subtype have been linked to dysfunctional HPA activation (Hong et al. 2003; Moss et al. 1995; Randazzo et al. 2008; Virkkunen 1985). However these findings are not completely consistent; for example, Van West et al. (2009) did not find a relation between low cortisol responsivity and psychosocial stress. These discrepancies however could be attributed to the study sample, design, comorbidity or treatment effects.

1.24 Chronotherapy for ADHD

If circadian rhythms are indeed altered in ADHD, and these alterations are linked to specific features of the condition, then interventions to re-synchronise the circadian cycles might then be particularly effective in alleviating these symptoms.

1.24.1 Melatonin

Several studies have examined the effect of melatonin treatment on ADHD symptoms and sleep related outcomes. The nature of the current evidence bases for the utility of melatonin in ADHD management include randomised, placebo-controlled and double-blind trials to longitudinal investigations on samples of ADHD or typically developing individuals (Coogan and McGowan 2017). Systematic administration of melatonin has been associated with significant decrease in sleep onset latency and increase in sleep duration among the participants (Masi et al. 2019). Tjon Pian Gi et al. (2003) reported a rapid decrease in sleep onset latency upon prior to bedtime administration of melatonin among children with ADHD and insomnia. Another earlier study even reported a decrease of sleep onset latency from 60 to 30 min as a

result of melatonin treatment for 4 weeks (Smits et al. 2001). Different studies have also argued regarding the best possible design and co-treatment that might lead to best sleep related outcome among the patients. Weiss et al. (2006) demonstrated that maximum reduction in insomnia symptoms took place when melatonin administration was coupled with sleep hygiene training. Similarly a decrease in sleep latency resulted from the co-administration of melatonin with methylphenidate, accompanied by an increase in the height and weight of the participating children (Mostafavi et al. 2012). Further, another study following a similar design of co-administering melatonin and methylphenidate showed decrease in sleep onset latency, but did not result in improvements of core ADHD symptoms (Mohammadi et al. 2012). Therefore, the above studies point towards the positive effects of melatonin in improving sleep onset among ADHD. Although for the above discussed studies, the treatment has not shown direct effect on the symptoms of inattention orhyperactivity. This finding should be interpreted keeping in mind that in such studies the role of parental input to manage concerns directly effecting sleep problems were not considered. Therefore, although Melatonin helped with sleep onset, the sleep issues that occur overnight, effect of comorbid symptoms, eg. Anxiety could still be impacting the child's sleep. When parents are better equipped at managing these problems in collaboration with the effect of Melatonin more generalized improvements in functioning may surface (Hiscock et al 2015).

With regard to delayed sleep phase, melatonin administration has shown some positive effects. A meta-analysis (Van Geijlswijk et al. 2010) reported that exogenous intake of melatonin leads to the advancement of the endogenous melatonin onset in both children and adolescents. In 2006, Szeinburg showed that a 6-month intake of melatonin resulted in shorter sleep latency and longer sleep duration among a group of children and adolescents diagnosed with delayed sleep phase syndrome. Melatonin treatment has shown advancement of DLMO, indicating melatonin's utility in correcting delayed circadian phase (Van der Heijden et al.

2007). One question of importance regarding melatonin in these studies is whether melatonin is deployed primarily as a somnolent or as a chronobiotic; the doses and timing of optimal treatments will differ accordingly, and as such this clear distinction should be made at the conception of studies (Arendt 2005b).

1.24.2 Behavioural Interventions

Behavioural chronotherapeutic interventions for treatment of circadian and/or sleep related concerns in ADHD populations over the last decade have shown some promise. Mullane and Corkum (2006) investigated the effect of behavioural intervention for sleep in three unmedicated children over a 5-week treatment period and found that the children's sleep improved and were maintained over a 3-month follow-up period. Corkum et al. (2009) validated the above findings on a larger randomised controlled trial (RCT), where the ADHD children were found to have significantly improved sleep as compared to typically functioning control group. The intervention included facets such as psychoeducation about basic sleep physiology and the different types of sleep problems/ disorders, sleep hygiene and bedtime routines, implementing a faded bedtime strategy and reward program (Mullane and Corkum 2006). Over the following period other well-designed RCTs also supported the effectiveness of behavioural interventions for the improvement of sleep concerns in ADHD sample of participants (Hiskock et al. 2015; Keshavarzi et al. 2014). Hiskock et al. (2015) found significantly improved ADHD symptoms (through parent and teacher ADHD rating scale), sleep problems (parent reported severity through children's sleep habits questionnaire and actigraphy), behaviour and daily functioning (measured through strengths and difficulties questionnaire) and working memory (working memory test battery for children) because of the behavioural sleep intervention-controlled trial. Similar results were also highlighted by Peppers et al. (2016) where sleep hygiene program led to better sleep quality and improved ADHD

symptoms.

1.24.3 Light

The use of morning bright light therapy among ADHD children has been shown to result in correction of delayed sleep phase and also improvements in ADHD ratings (Gruber et al. 2007). Similar findings (alleviation of core ADHD symptoms and improvements in affective symptoms) have also been demonstrated in case of adults that demonstrated that shifts towards earlier circadian preference were associated with improvement in the overall subjective and objective ADHD symptom ratings (Rybak et al. 2006). Other preliminary pilot findings further support the principle that light therapy as a chronotherapeutic may be useful in the management of ADHD symptoms: Fargason et al. (2017) report that morning bright light, coupled with the minimisation of evening bright light, advanced DLMO and was associated with decreased ADHD scores. Given the promise of light therapy in other areas of psychiatry and psychology (Cunningham et al. 2019), further study of this strategy in ADHD is warranted.

1.24.4 Agomelatine

Agomelatine is a licenced antidepressant in the European Union and Australia, which is an agonist of MT1 and MT2 melatonin receptor and an antagonist of 5-HT2c and 5-HT2B serotonin receptors that at least partially functions as a chronobiotic (Guardiola-Lemaitre et al. 2014). Preliminary evidence has suggested that agomelatine treatments lead to decreased ADHD-related symptoms (Niederhofer 2012). Salardini et al. (2016) reported in a study with a small group of ADHD children and adolescents that outcomes related to ADHD symptoms were not significantly better for the agomelatine-treated group than those treated with methylphenidate; however, the former reported less concerns associated with insomnia as a treatment outcome. Although these findings reveal some promise, concerns around hepatotoxicity with agomelatine and the lack of licensing in major jurisdictions are likely to

curtail interest in further exploring its use in ADHD, and future studies may rather focus on other melatoninergic agonists (Comai et al. 2019).

1.25 Sleep and ADHD: Continuing gaps and next areas of explorations

Certainly, it would appear that cognitive and behavioural strategies to improve sleep and/or circadian function in ADHD might be expected to yield benefit. Such trends have been visible in major depression where Cognitive Behavioural Therapy for insomnia (CBTi) results in significant and durable antidepressant effects (e.g., Kalmbach et al. 2019). Large trials of internet-delivered interventions indicate that CBTi results in improvements in psychopathology and quality of life (Espie et al. 2019). Thus, trials of CBTi in ADHD too might appear to be strongly warranted. Chronotherapy incorporating bright light therapy may also be a useful treatment modality and has shown much promise in other diagnoses (Cunningham et al. 2019). Further, circadian principles may be deployed in the pharmacotherapy of ADHD: either through the use of melatonin or melatoninergic agonists as chronobiotics, or through the use of circadian medicine to identify time-of-day for optimal effectiveness of psychostimulants used routinely in the treatment of ADHD (Ruben et al. 2019).

The current literature leaves a number of important questions, chief amongst these is whether circadian changes are symptoms of ADHD, or precursors to ADHD, or risk factors for ADHD, or a mix of these? There are some suggestions from recent longitudinal studies that suggest sleep disturbances preface and predict ADHD diagnosis in young children (Soehner et al. 2019; Tso et al. 2019). Indeed, there have been recent suggestions that ADHD might be reasonably reconceptualised as a sleep disorder, with ADHD features emerging (in part) as a neurocognitive result of chronic sleep disturbances and circadian changes (Bijlenga et al. 2019). Perhaps, the first question to answer the above query, (which will affect the research being undertaken in this project), should include: what is the nature of sleep difficulties in

childhood ADHD and what are the different biological, psychological and environmental factors that might be influencing the predisposing, precipitating and the perpetuating factors affecting the sleep related problems in the child.

Based on the scope of our research we want to first aim to comprehensively elaborate the nature of sleep difficulties in the child and then explore the possible ADHD related cognitive- behavioural facets, and environmental factors that might be influencing the child's sleep. Going through the chapters will also include some confounding variables that might influence the child's sleep.

Chapter 2:

A Systematic Review of Sleep and Circadian Rhythms in Children with Attention Deficit Hyperactivity Disorder

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Abstract

Children and adults with ADHD often report sleep disturbances that may form part of the etiology and/or symptomatology of ADHD. In this chapter we reviewed the evidence for sleep changes in children with ADHD. We conducted a systematic review of the extant literature to assess sleep and circadian functions in children aged 5 to 13 years old with a diagnosis of ADHD and developed a narrative synthesis. 148 studies were included for review, incorporating data from 42,353 children. We found that sleep disturbances in ADHD are common and that they may worsen behavioural outcomes; moreover, sleep interventions may improve ADHD symptoms, and pharmacotherapy for ADHD may impact sleep. Our review concluded that sleep disturbances may represent a clinically important feature of ADHD in children, which might be therapeutically targeted in a useful way. A number of important gaps in the literature were underlined, based on which we set out a manifesto for future research in the area of sleep, circadian rhythms, and ADHD.

2.1 Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder characterized by the core psychopathological features of inattention, hyperactivity and impulsivity, and is associated with poor psychosocial out- comes (McGough, 2014). Children diagnosed with ADHD exhibit goal directed behaviors, although these frequently are incomplete or inaccurate, resulting in impaired outcomes for academic, vocational and interpersonal interactions, accompanied by maladaptive psychological and physiological traits (Posner et al., 2020). ADHD, like other neurodevelopmental disorders, has been associated with sleep disturbances which may manifest as long sleep latency, sleep phase delay syn- drome, increased periodic limb movements during sleep, daytime sleepiness, altered total sleep duration and difficulty initiating and maintaining sleep (Ball, 1997; Corkum et al., 1998; Cortese et al., 2006; Konofal et al., 2001, 2010; Mayes et al., 2009). As sleep deprivation may exert multiple impacts on neurobehavioral and cognitive systems, including attention and emotional regulation (Krause et al., 2017), sleep disturbances in ADHD may affect the core psychopathology of the condition, and as such sleep-related factors may be important in the etiology of the condition. Further, sleep disturbances may arise from ADHD-related impulsivity and hyperactivity, and as such sleep problems may be part of the symptomatology of ADHD (Raman and Coogan, 2019).

Sleep is a highly complex, dynamic process involving multiple stages (including rapid eye movement (REM) sleep and non-REM stages) and may serve a number of essential, non-redundant functions (Scammell et al., 2017). In order to understand how sleep and ADHD may be related, it is important to examine key behavioral control systems that shape sleep physiology and sleep behavior. The sleep/wake cycle is shaped by the interaction of the circadian clock and the sleep homeostat (Borbély et al., 2016). The circadian clock is an

endogenous daily timekeeping mechanims that produces rhythms with periods of near 24 hours in a host of physiological processes (Vitaterna et al., 2001). Sleep homeostasis adjusts sleep processes to account for time spent in wakening and accumulated sleep pressure since the last consolidated sleep bout (Deboer, 2018). Dysfunction of the circadian system and/or the sleep homeostat may contribute to sleep problems in ADHD (Bijlenga et al., 2019). Studies of children, adolescents and adults with ADHD, utilizing both objective and subjective assessment of rest and activity cycles show significant variations in daily rhythms in behavioral, cognitive, endocrine, physiological and molecular processes, when com- pared to typically functioning individuals (Korman et al., 2019). Studies of circadian rhythms in adults with ADHD consistently report alterations in circadian phase, chronotype and other circadian parameters, indicating that the circadian clock may play an important role in adult ADHD (Coogan and McGowan, 2017).

As sleep and circadian function are profoundly influenced by life course (Roenneberg et al., 2007), there may be differential relationships of sleep, circadian rhythms and ADHD symptoms across the life course (Hegarty et al., 2019). This may be most marked during adolescence given the neurodevelopmental, behavioral and sleep-related changes that occur during this period (Pokhrel et al., 2013). As such, to gain a comprehensive insight into such relation- ships, it may be most useful to examine relatively narrow age ranges, especially in childhood and adolescence.

In the present review, we sought to synthesize the current evidence relating to sleep and circadian function in children between the ages of 5 and 13. We identified the need for such a review through a survey of the extant systematic reviews on sleep and/or circadian rhythms and ADHD via the Prospero and Cochrane registers of existing reviews in this field. The existing literature reviews in this topic either narrowly

concentrate upon discussing possible treatment strategies and therapeutic approaches (Alamar et al., 2015; Bioulac et al., 2015; Cortese et al., 2013; Hvolby et al., 2015; Nikles et al., 2020; Tsai et al., 2016), or review the relationships between specific sleep features and ADHD in smaller systematic reviews focused on specific sleep feautres (Martin et al., 2019; Mogavero et al., 2018; Polmann et al., 2020; Sadeh et al., 2006; Martins et al., 2019; Scarpelli et al., 2019; Walters et al., 2008). Further, a number of reviews focus generally on the pharmacotherapy of ADHD, and as such sleep issues are of secondary interest in these works (Abdelgadir et al., 2018; Cortese et al., 2018; Krinzinger et al., 2019; Punja et al., 2016; Storebø et al., 2016, 2018). Although, a selected group of reviews do explore sleep and circadian rhythms in ADHD, they do so for adult ADHD (Coogan and McGowan, 2017; Lugo et al., 2020; Díaz- Román et al., 2018; Wajszilber et al., 2018). Given that more than half of the ADHD diagnosis is made during childhood (Pastor & Reuben, 2008; Visser et al., 2010) clearly defining the changes in sleep/wake rhythms in the childhood ADHD population is vital. As such, we have identified a need for an up-to-date, systematic and broad review of the association of sleep and ADHD in childhood, and it is to this need that the current study is addressed.

2.2 Methods

The method of this systematic review was developed in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) criteria (Liberati et al., 2009). Given the wide variety of sleep and circadian rhythms measurements used in extant studies reviewed, and the broad nature of the review, we decided that metaanalysis would not be useful given the high level of methodological heterogeneity. Acknowledging this methodological heterogeneity in the current literature, limiting our study to a meta-analysis would limit our discussion to only a specific assessment modality, thereby restricting the scope of our project. Rather, we sought to systematically review the literature and conduct a narrative

synthesis.

Study Eligibility Criteria

For inclusion, studies must have had clearly identifiable cohorts of children between the age group of 5 to 13 years old with a diagnosis of ADHD through standardized diagnostic tools. We have restricted our participant criteria to ADHD diagnosed individuals because including a general population or clinical sample of children would lead to the overlapping presence of features characterizing different neurodevelopmental disorders, developmental delays and other psychiatric disorders. Any studies in humans that discussed findings of sleep or circadian functioning (subjectively or objectively measured through sleep logs, questionnaires, psychological tests, actigraphy, polysomnography or other physiological techniques) in cohorts with clinical assessment of ADHD symptoms were included for further reading, given that they adhered to the following: is an original, peer-reviewed and published paper that discussed empirical primary study findings (conference abstracts, book chapters, academic letters and reviews were excluded); the language of the article was English; and the publication date was between 1st January 2009 to 31st December 2019.

Search Strategy, Screening, and Extraction

We used the search logic ("Attention Deficit Hyperactivity Disorder" OR "ADHD" OR "Hyperkinetic disorder") AND ("Sleep" OR "Circadian" OR "Chronotype" OR "Actigraphy" OR "Polysomnography" OR "Diurnal Preference") to search PubMed, Embase, Web of Science and Clinical trials.org databases for studies published between 1st January 2009 and 31st December 2019. After recording search results from individual databases, all results were consolidated in the EndNote application and the first attempt at removing the duplicates from each database search was made. The resultant record of 2,540 studies were then uploaded to the Rayyan website (https://rayyan.qcri.org/), an online application for creating article databases for systematic reviews. From this initial group of studies, all study abstracts were screened to be filtered (based on previously decided inclusion criteria) in to "included", "excluded", "maybe" and duplicate categories. The "maybe" category was subsequently reviewed by all three authors to reach a consensus about being either included in the core review list of studied articles or completely excluded. Next, the "included" list of studies were further discussed in detail to filter out articles that were not congruent with the inclusion criteria.

Figure 2.1 includes the PRISMA flowchart representing the step-by-step exclusion leading to the final group of selected articles. The process of data extraction included the first author selectively mining the following information from the articles to form a master excel sheet of studies included in the core review list: study title; authors; study design; study objective; participant characteristics (including sample size, diagnosis, gender, ADHD medication use, and age); primary measures used; limitations and summary of main results.

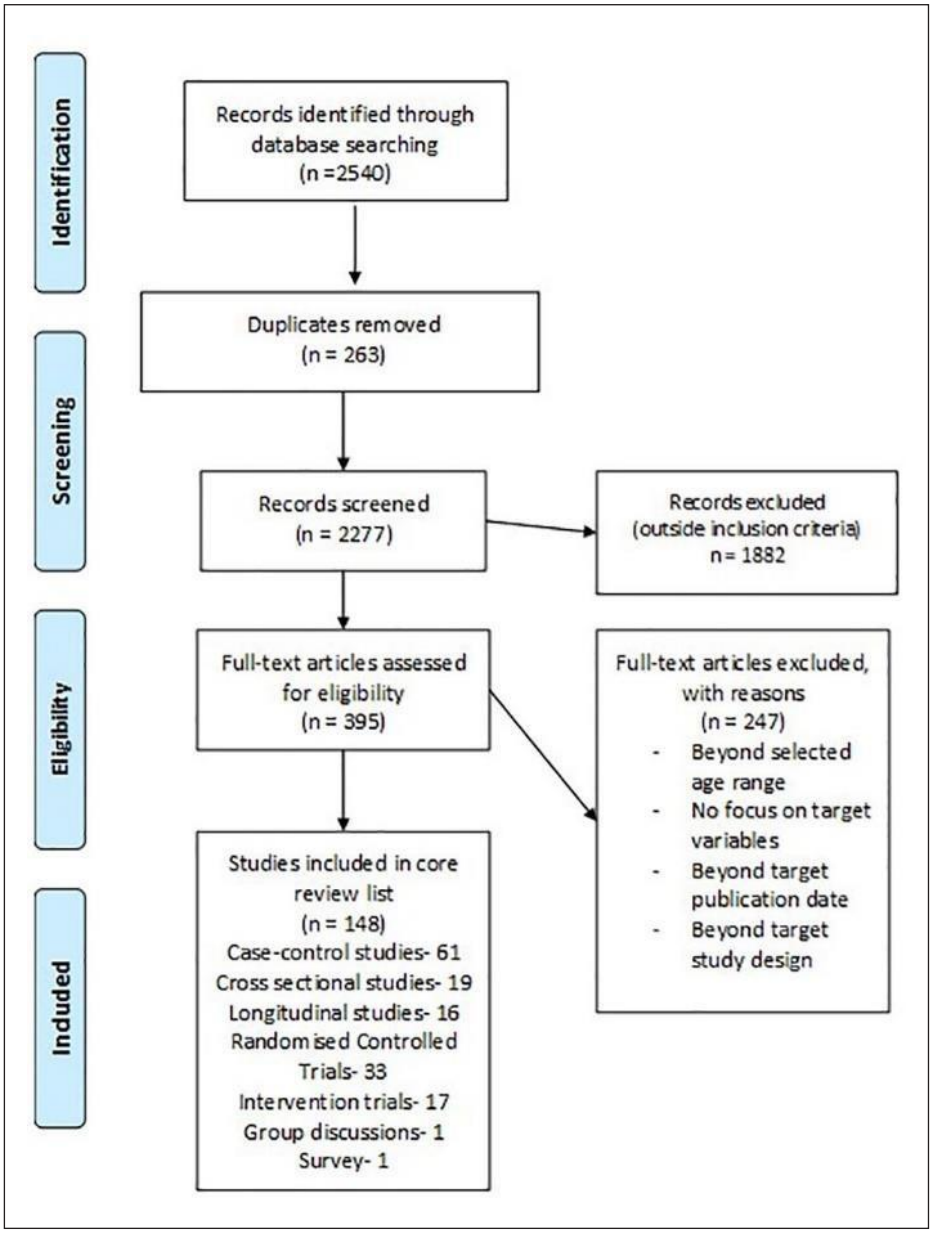

Figure 2.1

PRISMA flowchart representing the step-by-step exclusion leading to the final group of selected studies.

2.3 Results

Overall 148 articles were included for review, encompassing findings from a total 12427 children diagnosed with ADHD, 29,068 typically developing children and 858 children with other clinical/psychiatric conditions. The selected pool of articles consisted of 61 case control studies, 19 cross sectional studies and 16 longitudinal studies. For the psychological

and pharmacotherapy-based based intervention studies, 33 randomized controlled trials, 17 intervention trials, and 1 each of group discussion and survey method study were recorded. For structured review of these studies, we categorized them into five sections: (1) articles exploring sleep in children diagnosed with ADHD (Table 2.1, Table 2.2 and Table 2.3); (2) articles exploring circadian rhythms and chronotype in children diagnosed with ADHD (Table 2.4); (3) articles exploring functional consequences of sleep functioning in children with ADHD (Table 2.5); (4) articles exploring sleep-related interventions and their impact on sleep and daytime function in childhood ADHD (Table 2.6), and (5) articles exploring childhood ADHD pharmacotherapy effects on sleep (Table 2.7). Details from each study have been represented in separate tables below.

Sleep in Children Diagnosed with Attention Deficit Hyperactivity Disorder

Subjective assessment of sleep-in children with ADHD through Parental/caregiver/teacher reports

In this section the studies reviewed report differences in parent-rated sleep variable measures for children with ADHD when compared to a typically functioning group (study details provided in Table 2.1). Significantly higher parental ratings on the Child Sleep Habits Questionnaire (CSHQ) for bedtime resistance, sleep anxiety, parasomnias, sleep onset delay, sleep disordered breathing, daytime sleepiness and a global sleep disturbance score was found among children with ADHD when com- pared to age matched control group (Abou-Khadra et al., 2013; Chiraphadhanakul et al., 2015; Moreau et al., 2013). Exploring the above variables further, Lycett, Mensah, et al. (2015) found that a parent reported 7-day sleep log and CSHQ ratings revealed a distinct sleep pattern: children with moderate/severe sleep problems had shorter sleep duration (by −30 minutes), more night awakenings and longer sleep latency when compared to those with no/mild sleep problems. Additionally, Lycett, Mensah, et al. (2014)

found that among 195 children with ADHD (5–13 years), 49% had transient parental-reported sleep problems (assessed through CSHQ), whereas 10% were reported to have persistent sleep problems. For persistent sleep problems, risk factors were found to be internalizing and externalizing symptoms severity, medication use and ADHD symptoms severity, whereas for transient sleep problems, poor parental mental health and co-occurring internalizing and externalizing behaviours were found to be risk factors (Lycett, Sciberras, et al., 2014). Using the CSHQ, it was also found that elevated scores on individual subscales (sleep onset latency, night waking, day-time sleepiness, sleep duration, parasomnias, daytime sleepiness) among the ADHD cohort were positively associated with a variety of parent reported externalizing behavioural problems (social, attentional, and disruptive behaviours) and functional impairment (family, school, life skills, social activities and risky actions) (Aronen et al., 2014; Choi et al., 2010; Eyuboglu & Eyuboglu, 2018). Additionally, subjective reports by parents revealed that sleep problems emerging early for children (aged 6–8 years) with ADHD (n = 177) are uniquely associated with co-occurring internalizing and externalizing behaviors (Sciberras et al., 2016).

Williams and Sciberras (2016) report in a longitudinal study that children with mother-reported ADHD symptomatology had significantly more behavioral sleep concerns, along with poorer emotional and attentional regulation, and these features were evident from 2 to 3 years and remained poorer up to the age of 6 to 7 years (ADHD n = 112, ADHD symptomatic n = 648). In another longitudinal study of 5 to 14 year-old children, 4204 responses revealed parent-reported sleep problems “often” were independently associated with early remitter and persistent attention problems, and “some- times” associated with early remitter and adolescent onset attention problems (O’Callaghan et al., 2010). Persistence of parent-reported sleep problems with usual treatment after diagnosis was found not to differ for 39 children with ADHD (7–13 years) when measured at 2 time points (within 18 months, through the CSHQ)

with parent ratings above the clinical cut off score of 41 at both time points (Hansen et al., 2013), indicating that sleep problems may run a chronic course among children with ADHD.

Parent/caregiver-reported presence of sleep-related psychological problems have been found among children with ADHD (n = 30, aged 5–13 years), such as more incidence of anxiety, nightmares and needing the bedroom lights to be on (Gomes et al., 2014). Sluggish cognitive tempo was found to be associated with shorter sleep duration, poorer sleep, being harder to wake and becoming alert after waking in the morning among 147 ADHD-inattentive children aged 6 to 11 years (Becker, Pfiffner, et al., 2016). Hvolby et al. (2009) found that 13.3% of all children with ADHD(45) have nightmares, compared with only 1.4% of healthy children (212). It is also important to note here that parental ratings for 7 to 13-year-old children with ADHD comorbid with anxiety disorder (n = 25) revealed not only higher scores for CSHQ, but also higher occurrence of sleep anxiety and night waking (Hansen et al., 2011). Rodopman- Arman et al. (2011) found that among their ADHD sample of children (n = 40), about 22% (vs. 2.9% of the control group) needed their parents to accompany them while going to sleep, and transitional objects were needed by 8.1% of children with ADHD in contrast to 2.9% of controls (n = 40). Considering parent-reported sleep latency and total obtained sleep, significant differences have been observed in children with ADHD. In a group of 147 ADHD-predominantly inattentive (ADHD-I) children (aged 6–11 years), 14 percent were reported to achieve less sleep than recommended age- appropriate duration (7.5–11 hours), and 31% showed sleep onset latency greater than 20 minutes (Becker, Froehlich, et al., 2016). Similar findings were also reported by Hvolby et al. (2009) when 31% of children with ADHD (n = 45) were reported to be unwilling to go to bed, 22% had difficulty falling asleep and a greater proportion of children with ADHD had long sleep latency time compared to healthy controls (n = 212) and a non-ADHD psychiatric group (n = 64). Moreau et al. (2014) found that 41

children with ADHD (both medicated and un-medicated) had a higher score than the control group (n = 41) for the scale of Insomnia Severity Index for children (ISI-C).

Poorer ratings for sleep quality, duration and efficiency have also been reported for children with ADHD. Parents reported poorer total sleep quality scores on the Pittsburgh Sleep Quality Index (PSQI) for 28 children with ADHD (8–12 years) along with higher sleep latency and lower reported sleep efficiency when compared to the typically functioning group (Akinci et al., 2015). In this same study, increased scores for daytime sleepiness among the ADHD group were also reported. Children with ADHD (n = 15) have been reported to achieve shorter sleep duration and to be more restless in bed compared to controls (n = 36) (Andersson & Sonnesen, 2018). A longitudinal study of an ADHD cohort (n = 173) found a consistent decrease in sleep duration by one standard deviation to be a significant predictor of ADHD at 3 to 5 years; additionally, night waking was significantly present from the age of 5 years through to 9 years 7 months (Scott et al., 2013). Reynaud et al. (2018) found that both parent-reported night waking and inattention/hyperactivity trajectories were strongly correlated between 2 and 5 to 6 years (n = 1,324). Even for a younger age group, longitudinal study (ages 1.5 to 5 years, using self-administered questionnaires for the mothers of 2057 children), night time sleep duration and hyperactivity trajectories were highly inter-correlated (Touchette et al., 2009). The same study also found that children with shorter sleep duration and high hyperactivity scores were boys from low-income families and with mothers having low educational attainment. The link between shorter sleep duration and ADHD symptomatol- ogy was also reported when 411 parent–child dyads were assessed at two time points (Kindergarten and primary 3 in China, 5–9 years), revealing a higher risk of probable ADHD in primary 3 (as measured through parent rated questionnaire and DSM-V) for children who slept less than 8 hours during kindergarten, as opposed to those chil- dren who slept between 11 and 12 hours during kindergar- ten (Tso et al., 2019). Here the authors also found a higher prevalence of

probable ADHD among children who had 0 to 3 days of good quality sleep (during primary 3) as com- pared to the children who had 6 to 7 days of good quality sleep. A longitudinal analysis from childhood to early adulthood (n = 2,042) in a twin cohort (ADHD diagnoses at 5,7,10,12 and 18 years-old) revealed that children with ADHD had poorer sleep quality in young adulthood (self- rated by patient), but only if their ADHD persisted (Gregory et al., 2017).

Particular trends of parental reported sleep problems have been identified for individual ADHD subtypes. As compared to inattentive subtype, ADHD hyperactivity sub- type children received elevated ratings on the CSHQ (Eyuboglu & Eyuboglu, 2017; Grünwald and Schlarb, 2017). Grünwald and Schlarb (2017) also noted higher comorbid occurrence of insomnia and nightmares in this subgroup (6–13 years, n = 72). Subjective reports by paents revealed higher prevalence of sleep problems in children with ADHD combined presentation (30%) as compared to ADHD inattentive presentation (17%), however this finding was not statistically significant (Sciberras et al., 2016). However, in a previous study by Hansen et al. (2011), ADHD combined, and hyperactive subtype ratings did not differ from ADHD inattentive on theCSHQ scale (7– 13 years, n = 39).

Bessey, Richards, et al. (2013) studied parental attitudes and beliefs with regard to their ADHD child's sleep as compared to those held by parents of typically developing children.In this study, 84 respondents on the Sleep Attitudes and Beliefs Scale (SABS) were parents of children with ADHD, 92 of ASD (Autism Spectrum Disorder) children and 179 were parents of typically developing children (all children 5–12 years). Results indicated that compared to the TD children's parents, both ADHD and ASD children's par- ents reported that their child's sleep problems are less modifiable and responsive to change. A number of studies have focused on parent's own level of functioning and daily behaviors that might be associated with their children's sleep problems. Matsuoka et al. (2014) found a higher significant positive

correlation between parent reported total CSHQ scores for their ADHD/ASD children (n = 43, 6–12 years) and their own sleep quality's self-report using the Pittsburgh Sleep Quality Index (PSQI) when compared to parents of typically functioning children. In a cross-sectional study among 67 children with ADHD (5–12 years) Noble et al. (2011) found that parental-reported lack of consistent daily routine was a significant predictor for their child's bedtime resistance and along with that parenting stress was negatively correlated with daily implemented living routines and predicted sleep anxiety for the child with ADHD. Additionally, parent implemented daily living routine was correlated with the family's income and lower income parents tend to implement less consistent daily routines. Consistent with these findings, Sciberras et al. (2017) found that for 361 children with ADHD (5–13 years) greater parenting consistency and better sleep hygiene were associated with decreased bedtime resistance, while better sleep hygiene was associated with lower levels of daytime sleepiness, less delayed sleep onset (associated with greater parental warmth), and fewer sleep duration difficulties.

Objectively measured macro-structural properties of sleep among children with ADHD

Several studies have utilized actigraphic measures for the estimation of total sleep time and sleep latency among children with ADHD (studies detailed in Table 2.2). Case control investigations have revealed shorter sleep duration and longer sleep latency among children with ADHD compared to the typically developing control group (Lee et al., 2014; Miano et al., 2019; Moreau et al., 2013). Moreau et al. (2013) also found that children with ADHD (n = 43, 6–13 years) with comorbid psychiatric conditions had significantly longer sleep onset latency when compared to the ADHD-only group or the control group. When total sleep time is considered, it was also found that children with ADHD with comorbid conduct dis- order (n = 16) slept significantly less than children in the control group (n = 30) and those with only conduct disorder (CD= 4) as measured through actigraphy (difference of 50 minutes; Aronen

et al., 2014). Contrary to the above findings, Wiebe et al. (2013), Bergwerff et al. (2016) and Waldon et al. (2018) found no significant difference in actigraphy-measured total sleep time and sleep latency for children with ADHD as compared to typically developing control groups. The study by Waldon et al. (2018) also found that sleep duration significantly predicted performance on an objective attention test in both children (6–12 years) with ADHD (n = 25) and TD (n = 25) children but did not significantly predict parent-reported attention supporting that poor sleep would predict poor attention regardless of whether or not the child had ADHD (Waldon et al., 2018). For night-to-night variability in actigraphic sleep parameters among 7 to 12-year-old ADHD (n = 50) and typically developing children (n = 50), significant difference in sleep duration was only found among the different nights, but the difference was not significant between the ADHD and the control group (Poirier & Corkum, 2018). However, if the presence of comorbid CD/ODD is considered, Bergwerff et al. (2016) found that for time in bed, significant interaction effects were found between the aggregated ADHD measure and parent and teacher rated CD and Oppositional defiant disorder (ODD) (n = 63, 6–13 years); similarly, for total sleep time significant interactions between the aggregated ADHD measure and parent and teacher rated internalizing and CD/ODD behaviour.

For sleep efficiency quantitated through actigraphy recordings, children with ADHD (n = 43, 6–13 years) were found to have significantly lower sleep efficiency compared to healthy control group children (Moreau et al., 2013). Children (7–12 years) with ADHD and comorbid conduct disorder (n = 16) had significantly lower sleep efficiency than both children in the control group (n = 30) and those with only conduct disorder (n = 14) (Aronen et al., 2014). However, Lee et al. (2014) found no significant difference in sleep efficiency between the ADHD group (n = 37) and typically developing peers (n = 32) in the same age group. When sleep actigraphy results at home and sleep lab were compared for 25 children with ADHD (6–12 years) with age matched control group, both groups slept 50 minutes less in the sleep lab

and sleep efficiency was improved for the typi- cally developing group (n = 25) in the sleep lab conditions, but not for children with ADHD (Bessey, Coulombe, et al., 2013).

Assessment of restlessness or movement during sleep measured through actigraphy has indicated increases in the sleep fragmentation index among children with ADHD in a number of studies. Wake after sleep onset (WASO) refers to periods of wakefulness occurring after defined sleep onset (Shrivastava et al., 2014) and has also been explored in a number of studies with children with ADHD. When compared to typically developing 7 to 12 years-old children (n = 32), children with ADHD (n = 37) were found to have more WASO and higher fragmentation index scores (Lee et al., 2014). For children with ADHD, error and response latency rate on an objective test of impulsivity was also positively correlated with the WASO and fragmentation index (Lee et al., 2014). Mean activity count per wakening epoch after sleep onset are also reported to be elevated in children with ADHD compared to typically developing children and higher still in children with ADHD and comorbid psychiatric condition. However, Bergwerff et al. (2016) found no significant difference in actigraphic measures of nocturnal motor activity for children with ADHD (n = 63) as compared to typically developing control group (n = 61).

Objectively measured micro-structural properties of sleep in children with ADHD

A number of studies have studied Rapid Eye Movement (REM) sleep characteristics measured by nocturnal polysomnography (PSG) in children with ADHD (studies detailed in Table 2.3). Akinci et al. (2015) found that 8 to 12-year-old children with ADHD (n = 28) had a lower percentage of REM sleep compared to healthy controls (n = 15). A home PSG also found significantly shorter duration of REM sleep, smaller percentage of total time spent in REM sleep and shorter sleep duration, in the ADHD group (n = 15) compared to control group (n = 23) children aged 7 to 11 years (difference of ~15min per night in REM sleep; Gruber et al., 2009). Díaz-Román and Buela-Casal (2019) report that similar age group children with ADHD (n = 20) had shorter REM latency compared to typically developing children (n = 20) and Grissom et al. (2009) found that 6 to 10-year-old children with ADHD (n = 13) showed significantly lower frequency of eye movement during REM sleep compared to the control group (n =16).

For Non-REM (NREM) sleep properties in children with ADHD, Akinci et al. (2015) report lower cyclic alternating pattern (CAP; periodic EEG activity which recurs at intervals up to 2 minutes), proportion of sleep time spent in total NREM and in Stage 2 (N2) sleep along with reduced A1 index (high voltage slow wave EEG activity) in N2 as well as shorter sequence mean duration and lower CAP rate A1. The authors also found that children with ADHD (n = 28, 8–12 years) had had lower SpO2 (Saturation of Peripheral Oxygen) and NREM SpO2 (both being significantly correlated to the Sleep Quality subjective measure, PSQI). Grissom et al. (2009) found that children with ADHD (n = 13, 6–10 years) had significantly lower percentage for stage 2 sleep when compared to controls and conversely that they had significantly higher percentage of stage 3 sleep when compared to controls. In line with the above findings, Silvestri et al. (2009) found significant differences in almost all of the studied sleep variables (REM%,

N3% N2%, N1%, SE% (sleep efficiency), TST (total sleep time) MIN, REM Latency, SLEEP Latency) between 55 children with ADHD and 20 controls (6–12 years). Markovska-Simoska and Pop- Jordanova (2017) found children with ADHD have increased absolute power of slow waves (theta and delta) as compared to matched controls. When the power of slow sleep spindles during stage 2 NREM sleep was evaluated, Saito et al. (2019) found that the ratio of 12-Hz frontal spindle power was higher in 5 to 13-year-old ADHD (n = 21) than in the typically developing children (n = 18) (especially for children with ADHD with comorbid ASD), and also that the ratio of 12-Hz spindles was significantly correlated with reaction time variability on a CPT to mea- sure attention. EEG power spectral analysis revealed significant differences concentrated in the period immediately after spindle epochs, in the left hemisphere of the brain, in almost all bands, with greater values in control (n = 7) than in children with ADHD (n = 8) among 6 to 10 year olds (De Dea et al., 2018).

Topographical distribution of Slow Wave Activity (SWA) recorded through high definition EEG nocturnal recordings in children with ADHD revealed a local increase of SWA in a cluster of six electrodes over central regions in 6 to 12-year-old children with ADHD (n = 9) compared to control (n = 9) children, indicating a less mature topographical SWA distribution in comparison to healthy children of the same age and sex (Ringli et al., 2013). In another study, full night high-definition PSG assessment of children with ADHD revealed a decrease of SWA during the night, with a focus of SWA over the centro–parietal–occipital regions and greater delta power over the posterior cingulate in participants with ADHD (n = 30, 7–13 years) (Miano et al., 2019). However, there is a level of inconsistency in the literature regarding sleep EEG findings in children with ADHD. Příhodová et al. (2012) found no significant differences in any of the CAP parameters between 7- and 12-year children with ADHD (n = 14) and controls (n = 12). On simi- lar lines, in an earlier study, Choi et al. (2010) found no significant differences between ADHD and healthy groups in any of the

polysomnographic sleep measures. Again, when studying the effect of stimulant medication (MPH) on sleep architecture in 27 children (6–12 years) with ADHD, Galland et al. (2010) found that sleep architecture was preserved, and the arousal indices remained unchanged.

PSG has also been used to assess other sleep features in children with ADHD. Multiple Sleep Latency test (MSLT) using PSG measures among 7 to 11-year-old children with ADHD revealed that longer time in slow-wave sleep were positively related to mean sleep latency and longer actigraph-measured time awake and more actigraph-measured activity were associated with longer mean latency on the MSLT (Wiebe et al., 2013). In another MSLT study, although mean sleep latency showed no inter-group differences between the ADHD (n = 31) and control group (n = 26), for the ADHD group a significant inter-test variability was observed, that is sleep latency values displayed statistically significant differences between some of the tests during the day (between the 1st and the 2nd,4th and 5th test) (Prihodova et al., 2010).

Miano et al. (2019) report that children with ADHD (n = 30, 8–12 years) showed a higher Apnea- Hypoapnea Index (AHI) than control group children (n = 25). The particular functional importance of sleep-disordered breathing in children with ADHD was shown in a study in which 61 (8–13 year old) children with ADHD with or with- out obstructive sleep apnea underwent an oddball auditory attention test coupled with detection of P300 (Event related potentials) followed by an all-night PSG, and revealed significant decreased amplitude of the P300 potential in children with Obstructive sleep apnea (OSA) +ADHD, when compared with children with only ADHD (Henriques Filho, 2016). However, there is not complete concordance between studies in this area: a two night PSG data (6–12 years) revealed no significant differences between control group (n = 28) and children with ADHD (n = 28) for presence of an AHI >1 (where a threshold of >1 AHI event per hour is of clinical relevance) orsnoring (Galland et al., 2011). . Further,within the same age group, Prihodova et

al. (2010) found no significant difference in the occurrence of sleep disordered breathing between ADHD (n = 31) and control children (n = 26) following a 2 night PSG and MSLT study.

Discussing beyond the papers reviewed in this chapter, per the recommended American Academy of Sleep Medicine scoring manual for Obstructive Sleep Apnea, the careful account of OSA (Obstructive Sleep Apnea) symptoms are vital, so that patients with excessive daytime sleepiness, insomnia or other specific neurocognitive symptoms can be correctly diagnosed (Malhotra et al 2018). Precenzano et al (2016) found that children with OSA have more hyperactivity, ADHD total index score, emotional dysregulation and restlessness when compared to the control group. On the other hand, out of 30 drug naïve ADHD diagnosed children, 15 were found to have OSA (Miano et al 2018). Therefore not only are sleep and neurocognitive problems seen in ADHD are also seen in OSA, additionally the prevalence of sleep apnea itself is pronounced in children with ADHD (Urbano et al 2021). Treatment for sleep apnea (e.g. adenotonsillectomy) have additionally shown improvements for ADHD subjective rating scales (Marcus et al 2013), thereby solidifying the bidirectionality between the two.

With regards to periodic limb movements recorded during PSG, Akinci et al. (2015) found that the periodic limb movement index (PLMI) was higher in children with ADHD (n = 28) compared to the control group (n = 15). Prihodova et al. (2010) found no significant difference in the occurrenceof periodic limb movements in sleep between 6 and 12-year- old ADHD (n = 31) and control (n = 26) children following a 2 night PSG and MSLT study, although a statistically signifi- cant difference was found in the trend for periodic limb movement index (PLMI) between twonights (a decrease of PLMI in the ADHD group and an increase of PLMI in the control groupduring the second night).

Table 2.1 *Summary of Thirty-One Included Studies Focusing on Subjective Measures of Sleep in ADHD.*

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male% female%)	Medication use	Age	Primary measures, limitations, andbiases	Objectives	Summary of main results: Interventions/comparisons/ outcomes
Abou-Khadra et al. (2013)	Case control	103 (ADHD: 41, control: 62)	85.4%/14.6%	Not currently medicated.	6–12 years	CSHQ, CPRS-R: L, Ferritin AccuBind ELISA test. Limitations: Small sample size, parent reports might lead to over-under estimation of sleep concerns and symptom severity, psychiatric clinic cases of ADHD might differ from community children with ADHD.	To examine the relationship between parent reported sleep problems, symptom-ratings, and low serum ferritin levels among Egyptian children with ADHD.	ADHD group showed significantly higher scores in CSHQ subscales (bedtime resistance 11.9±3.0 vs. 9.4±2.2, $p<.001$), sleep anxiety (8.0±2.4 vs. 6.1±2.0, $p<.001$), parasomnias (11.9±2.9 vs. 9.6±3.3, $p=.001$), sleep-disordered breathing (4.6±1.9 vs. 3.9±1.5, $p=.046$), daytime sleepiness(15.9 ±3.5 vs. 14.2±3.3, $p=.018$) and total scale score (60.0±10.4 vs. 51.5±9.2, $p<.001$) and negative association between low serum ferritin levels and sleep disturbances ($r=-.363$, $p=.020$).
Moreau et al. (2014)	Case control	ADHD: 41, control: 41	58.5%/41.5%	31 ADHD children on medication (Psychostimulants and Atomoxetine),10 not currently medicated	6–13 years	Actigraphy, Sleep Diary, CSHQ (Child Sleep Habits Questionnaire), BRIEF (Behavior Rating Inventory for Executive Functions), Conner's CPT (Continuous Performance Test), CPRS (Conner's Parent's Ratings Scale), K-SADS (Kiddie- Schedule of Affective Disorders and Schizophrenia), Insomnia Severity Index for children (ISI-C). Limitations: Almost one-half of thesample was composed of children with predominantly inattentive subtype, rating scales used to define comorbidity might not be accurate, given the small sample size, only ten children were unmedicated.	To examine the sleep of children with ADHD, using actigraphy and parental questionnaires,and examine the potentially moderating role of psychostimulant medication and psychiatric comorbidity.	Children with ADHD significantly differed (with higher scores) from controls on(CSHQ total score 42.75±6.27 vs. 37.49±3.70, $p<.001$), sleep onset delay(1.68 ± .79 vs. 1.17 ± .50, $p<.01$), sleep anxiety (5.77± 1.66 vs. 4.55±1.04, $p<.001$), parasomnias (8.80±1.56 vs. 7.91 ± 1.04, $p<.01$), daytime sleepiness(11.08 ±3.14 vs. 3.93 ± 2.61, $p<.05$), ISI-C total score (9.36±5.66 vs. 3.01±2.69, $p<.001$) and actigraphic measures of sleep (total sleep time (466.4± 40.6 vs. 490.6±33.3, $p<.01$), sleep onset latency (32.7±16.13 vs. 20.81±10.07, $p<.001$), sleep efficiency (79.21 ± 4.99 vs. 82.03 ± 3.71,$p<$ .01), mean activity counts per epoch (22.28 ±10.15 vs. 14.11±4.94, $p<.001$).
Chirapadhanakul et al. (2015)	Case control	ADHD: 55, control: 110	81.8%/18.2%	27 ADHD children on medication (short or long acting MHP)	5–12 years	CSHQ (Thai version), the ADHD rating scales, and the Strengthsand Difficulties Questionnaire (SDQ). Limitations: Sleep difficulties obtained by only parent report, marginal significance in father's education and income between bothgroups of study participants, and thelack of psychometric validation of the CSHQ–Thai version.	To compare the sleep disturbances in Thai children aged 5–12 years with ADHD and typically developing children using the Children's Sleep Habits Questionnaire (CSHQ)–Thai version.	Children with ADHD had significantly higher scores in all subscales of the CSHQ (@ $p<.05$) and 58.2% of ADHD children with higher SDQ scores (>15) appeared to have moresleep disturbances (including bedtimeresistance (mean±SD=12.55±2.62 vs. 10.52±2.63, $p=.005$), sleep anxiety (mean±SD=8.23±2.06 vs. 6.30±2.05, $p=.003$), parasomnias(mean ±SD=10.41±3.72 vs. 8.84±1.53, $p=.036$), and total sleep disturbances (mean ± SD = 55.81 ± 7.18 vs. 49.14±5.93, $p=.001$) on the CSHQ).

(continued)

Table 1. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objectives	Summary of main results: Interventions/comparisons/ outcomes
Lycett, Mensah,et al. (2015)	Cross sectional	ADHD: 392	85%/15%	313 ADHD children on medication	5–13years	7-day sleep log, CSHQ, ADHD-RS-IV, sleep problems severity assessment, Depression anxiety stress scale, Anxiety Disorders Schedule for Children-IV, Socio-Economic Indexes for Areas. Limitations: All sleep measure's reliance on parental report reflect common effect of parental perception acrossthe measures, findings limited to behavioral sleep problems, two- thirds of parents returned the sleep log, which may have under- or over-ascertained problem sleepers.	To compare parent reporton a global measure of the severity in child sleep problem (no/mild vs. moderate/severe) with parent report on a 7-Day Sleep Log and theCSHQ.	Sleep log data identified 2 distinct sleep patterns according to parent-reported sleep problem severity (no/mild & moderate/severe). Children with moderate/severe sleep problems slept, on average, 30 minutes less per night; and were more likely to experience night awakenings and had more problematic scores (effect sizes: .5–1.1) across all domains of CSHQ in comparison to those with no/mild sleep problems.
Lycett, Mensah,et al. (2014)	Cross sectional	ADHD: 195	87.2%/12.8%	152 ADHD children on medication (Psychostimulants and Atomoxetine)	5–13years	CSHQ, subjective sleep problems reported, Anxiety Interview Scheduleforchildren/parent, ADHD rating scale-IV and Depression Anxiety Stress Scale for caregiver. Limitations:children in persistent sleep problemstrajectory was small (n = 20), leading to insufficient power to demonstraterelationships precisely, age range of children spanned 9 years; therefore study unable to examine age-specific sleep problem trajectories, sleep medication (e.g., melatonin) data were not available at all three time points; thus, it is difficult to determine whether use of sleep medication altered trajectories.	To examine behavioral sleep problem trajectories, types of sleep problems experienced, and associated risk/ protective factors among ADHD children.	Sleep problems in children with ADHD are commonly transient, but in a subgroup they are characterized as persistent. Themost common trajectory was transient (49%; 95% CI 42, 56), followed by never (41%; 95% CI 34, 48) and persistent (10%; 95% CI 6, 15).
Choi et al. (2010)	Case control	ADHD: 27, control: 26	88.9%/11.1%	Medication naïve.	7–12years	CSHQ, CBCL (Child Behavior Checklist), K-SADS-PL-K, PSG. Limitations: PSG results not controlled for first-night effect in children with ADHD who are more sensitive to changes in environmentthan controls, children got only 6 hours sleep on the night of the N-PSG compared to 9 hours at home, small sample, mainly boys, correlation coefficients were smalland the relationship was modest.	To assess sleep characteristics in children with ADHD through polysomnographic recordings and parental reports of sleep problems.	Reported sleep problems were significantly associated with almost all subscales of CBCL as well as CBCL total score (between parasomnia and withdrawn$r$= .286, p<.05, between total sleep disturbance and withdrawn r=.290, p < .05, between somatic complaints and total sleep disturbance r = .331, p < .05, between anxious/depressed and total sleep disturbance r =.366, p<.01 between social problems and total sleep disturbance$r$ = .331, p < .01 between attention problems and total sleep disturbance r=.331, p<.01, between aggressive behavior and total sleep disturbance r = .376, p < .01, between externalizing score and total sleep disturbance r=.374,p < .01, between CBCL total score andtotal sleep disturbance r=.429, p<.01.

(continued)

Table 1. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations andbiases	Objectives	Summary of main results: Interventions/comparisons/ outcomes
Eyuboglu and Eyuboglu (2018)	Case control	ADHD: 83, control: 106	77.1%/22.9%	Participants not currently medicated.	6–12years	Conner's parent questionnaire, CSHQ, Weiss Functional Questionnaire. Limitations: ODD was not excluded, restless leg syndrome and periodic leg movement disorder were not evaluated, all scales were completed by parents; thus not controlling effectof parental perception on measures, family sleeping attitudes, daily physicalactivity, and use of electronics before bedtime were not examined.	To evaluate sleep problems of un-medicated children with ADHD and to investigate the effects of these problems in functionality.	Children with ADHD experienced more sleep problems and slept lessthan healthy children (total sleep disturbances mean ± SD = 56.3 ± 10.2 vs. 42.9 ± 6.1, $p < .001$ on CSHQ; amountof sleep (hours) mean ± SD = 8.5 ± 1 vs. 10.3 ± 1.2, $p < .001$.), and functionalimpairments increased due to these problems ($r = .707$, $p < .001$).
Aronen et al. (2014)	Case control	CD & ODD: 30 (16 comorbid ADHD), control: 30	90%/10%	11 children with ADHD on medication (Risperidone and MPH)	7–12years	K-SADS, CSHQ, Actigraphy. Limitations: Small sample size, likely limiting the statistical powerof the tests used, the actigraphic measurement time (3 nights) was only modest.	To compare the self- and parent-reported sleep problems and objectively measured sleep amount and efficiency in child patients with ADHD/ CD/ODD and their age- and gender-matched controls.	Children with comorbid ADHD slept significantly less than did thepatients with CD/ODD alone andthe controls (total sleep minutes mean ± SD = 500.3 ± 50.2 (ADHD+CD/ ODD) vs. 416.3 ± 59.8 (CD/ODD), $p < .001$ as measured through actigraphy).
Sciberras et al. (2016)	Case control	ADHD: 177, control: 212	68.93%/31.07%	21 children with ADHD on medication (MPH)	6–8years	Subjective questions for sleep problems, Daignostic Interview schedule for children-IV, BMI z-score, Child health questionnaire. Limitations: Measures of sleep, physical injuries and global health were brief and reported solelyby parents, unable to verify the type of sleep problem(s) experienced by children, number of children in our subgroup analyses examining differences by ADHD subtype was small, which may have led to insufficient power to demonstrate relationships precisely.	To examine health-related impairments in young children with ADHD and non-ADHD controls.	Children with ADHD had increased odds of moderate/large sleep problems (OR:3.1; 95% CI 1.4, 6.8), compared with controls.
Williams and Sciberras (2016)	Longitudinal	ADHD: 112, ADHD symptoms: 648, No ADHD: 3349	75%/25%	68 children with ADHD on medication (MPH)	Birth-7years	Sleep problems, emotional dysregulations and attentional regulation measured through mother reported specific questions, Strengthsand Difficulties Questionnaire (SDQ). Limitations: Single-item measure of sleep problems does not allow for specificity in identifying particular sleep behaviors that contribute most to daytime functioning and development of self-regulation skills over time, relying on mothers' reportalone leads to data being confounded with parental mental health and their own experience of ADHD symptoms.	To examine mean level differences and longitudinal and reciprocal relations among behavioral sleep problems, emotional dysregulation, and attentional regulation across early childhood for children with and without ADHD at 8 to9 years.	Sleep problems in children with and without ADHD are associated with emotional dysregulation and poorer attentional functioning (between sleep problems at 0–1 year and emotional dysregulation at 0–1 year, $r = .37$, between sleep problems at 2–3 year and emotional dysregulation at 2–3 year$r = .18$, between sleep problems at 4–5 year and emotional dysregulation at 4–5 year $r = .21$, between sleep problems at 6–7 year and emotional dysregulation at 6–7 year, $r = .23$ ($p < .05$) and between sleep problems at 4–5 year and attention regulation at 4–5 year, $r = .14$ ($p < .05$).

Table 1. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objectives	Summary of main results: Interventions/comparisons/ outcomes
Hansen et al. (2013)	Cross sectional longitudinal	Clinical grp.: 105 (out of which ADHD: 39, ADHD+Anx.: 25, Anx.: 41), control: 31	65.8%/34.3%	Not currently medicated.	7–13 years	semi-structured interview, Kaufman Schedule for Affective Disorders and Schizophrenia, CSHQ. Limitations: Small sample size, leading to lack of statistical power, lack of information regarding pubertal (pubertal onset related to sleep problems), use of only parent's report of sleep problems and not the child's report or objective sleep measures.	To examine the persistence and predictors of sleep problems over 18 months in children with anxiety disorders and/or ADHD and non referred controls.	Sleep problems may run a chronic course among children with ADHD (Restless sleep persisted in 32 children (persistencerate 72.7%), enuresis in 4 (persistence rate 66.7%), sleep talking in 22 children (persistence rate 68.8%), sleepwalking in 4 (persistence rate 57.1%), bruxism in 9 (persistence rate 60.0%), nightmares in 11 (persistence rate 50.0%) and night terrors in 2 (persistence rate 40.0%).
O'Callaghan et al. (2010)	Longitudinal	4204 parent responses	51.7%/48.3%	Not currently medicated.	5–14 years	Subjective questions for sleep problems, CBCL. Limitations: all reports of sleep and attention were through maternal reports and as such may be subject to bias, loss to follow-up may have led to biased estimates, without supportive clinical measures.	To examine whether sleep problems in infancy and early childhood are independently related to attention difficulty at 5 and 14 years, and to the continuity of attention difficulties from 5 to 14 years.	Sleep problems experienced "often" in early childhood are an indicator of subsequent attention problems that may persist into adolescence (odds ratio at 95% confidence interval, 1.84 (1.25, 2.70).
Gomes et al. (2014)	Case control	Hyperkinetic disorder: 30, Control: 30	83.3%/17.6%	13 children with ADHD on medication (MPH)	5–13 years	Portuguese Wechsler Intelligence Scale for Children, 3rd edition (WISC-III) or the Portuguese Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R), Child Waking questionnaire (CSWQ). Limitations: Sleep questionnaire did not address restless leg syndrome(RLS), limited clinical sample size leading to low statistical power, HKD sample followed ICD-10 criteria rather than DSM, children were not diagnosed through structured interviews, but instead according to a routine clinical evaluation by a child and adolescent psychiatrist.	To compare the parent-reported sleep of children with ICD-10 hyperkinetic disorder (HKD) versus community children.	ADHD)/HKD children may thus have more sleep-related problems than typically developing children (bedtime school nights median (mean) = 21.30 (21.47) vs. 21.30 (21.12), $p < .01$; bedtime school nights Sleep-median (mean) = 21.30 (22.34) vs. 22.00 (21.56), $p<.05$; sleep length school nights median (mean)=09.30 (09.07) vs. 10.00 (09.46), $p<.01$; sleep length weekend nights median (mean)=09.30 (09:38) vs. 10:00 (10:15), $p<.05$; willingness to go to bed median (mean)=2.00 (2.33) vs. 4.00 (3.47), $p<.001$; bedtime refusal median (mean)=2.00 (2.30) vs. 1.00 (1.27), $p<.001$ measured through parent reports.
Becker et al. (2016)	Cross sectional	ADHD-I: 147	59%/41%	6 children with ADHD on medication (MPH-washout period 1 week before study commenced)	6–11 years	Child Symptom Inventory-4, K-SADS, Parent Inventory of Children's sleep habits. Limitations: All measures were completed by parents, the sleep measure used not been psychometrically validated, and objective measures of sleep (e.g., actigraphy, polysomnography) were not obtained, laboratory testing of endocrinological or metabolic factors that could cause/contribute to SCT/sleep disturbance were not conducted.	describe the sleep habits of children diagnosed with ADHD Predominantly Inattentive Type (ADHD-I), and (2) examine whether comorbid internalizing, oppositional, and/or sluggish cognitive tempo (SCT) symptoms are associated with poorer sleep functioning in children with ADHD-I.	Comorbid anxiety, in addition to sleepy/ tired symptoms, were most consistently associated with poorer sleep functioning in children with ADHD-I (beta coefficient of .35 for Anxiety for poor sleepers @ $p<.001$ and beta coefficient of .20 for sluggish cognitive tempo for poor sleepers @ $p<.05$, R squared .20).

(continued)

Table 1. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objectives	Summary of main results: Interventions/comparisons/ outcomes
Hvolby et al. (2009)	Case control	ADHD: 45, control: 217, other psychiatric diagnoses: 64	82.2%/17.8%	Stimulant medication naïve	5–11 years	Children Sleep Behavior Scale, K-SADS-PL. Limitations: parents not asked whether they view child'ssleep difficulty as a sleep disorder, information regarding symptoms of breathing problems (SBD) or restless leg syndrome, possible psychiatric symptoms or ADHD-like behavior in the healthy control group were not assessed.	to describe sleep patterns and problems of 5–11-year-old children with ADHD described by parental reports and sleep questionnaires.	The ADHD group report problems with bedtime resistance, problems with sleep onset latency (in minutes) mean and SD, 44.3 (21.4) vs. 24.8 (11.1) $p<.001$, unsettled sleep and nightmares more often than the control groups.
Hansen et al. (2011)	Case control	Anxiety disorder: 41, ADHD: 39 comorbid condition:25), controls: 36	76.9%/23.1	Not currently medicated.	7–13 years	K-SADS, CSHQ. Limitations: Small sample size, only mother report, not self-report or sleep diary, was usedto assess sleep problems, and the questionnaire assessed only the most recent typical week, diagnoses based on parent interview, and this could lead to under-reporting of anxiety symptoms in children with ADHD as well as ADHD symptoms in children with anxiety disorders.	To compare sleep problems in the referred children diagnosed with an anxiety disorder, ADHD, comorbid anxiety disorder and ADHD, and non-referred controls.	Night waking was associated with comorbid anxiety disorder and ADHD more than control (mean,CI)- 4 (3–8) vs. 3 (3–5), $p<.001$, effect size .67); bedtime resistance was associated with anxiety disorder, more than control (mean,CI)- 8 (6–17) vs. 6 (6–14), $p<.001$, effect size .43), while daytime sleepiness affected all clinical groups (mean,CI)- 12 (6–20) vs. 9 (6–17), $p<.01$, effect size .35, for ADHD>CTRL).
Rodopman-Arman et al. (2011)	Case control	ADHD: 40, control: 40	80%/20%	Not currently medicated.	7–13 years	CSHQ. Limitations: Subjective measures of parental reports were used rather than objectively collected sleep measures, lower incidence level for ODD comorbidityin sample, patients with psychiatric comorbidity excluded.	To investigate the sleep habits, associated parasomnias and behavioral symptoms in primary school children with ADHD.	Children with ADHD had more problematic sleep habits and night-time associated behaviors than controls. For example, sleep latencies of children with ADHD during the weekdays (21.6 ± 22vs 15.8±12.8 (in minutes±SD), p: .03) and on weekends (21.6±19.1 vs. 14.9±11.7 (in minutes±SD), p: .001) were longer than in the normal controls. Similarly, rates of nightmares (p: .001), nocturnal enuresis (p: .001), habitual snoring (p: .007), and restless sleep (p: .02), daytime sleepiness ($p<.001$) were higher in children with ADHD.
Moreau et al. (2013)	Cross sectional	ADHD:43	58.1%/41.9%	31 children with ADHD on medication (extended and immediate release psychostimulants, Atomoxetine and psychostimulants + Atomoxetine.	6–13 years	Conner's Continuous Performance Test (CPT), Actigraph, Sleep diary, CSHQ, Conner's parent rating scale, K-SADS, BRIEF (Behavior Rating Inventory of Executive Functions. Limitations: Small sample size, heterogenous in terms of medication use, half of sample had inattentive subtype only, due to cross-sectional nature, causality between sleep disturbances and daytime functioning measures cannot be inferred.	To investigate potential relationships between two measures of sleep impairments (i.e., sleep duration and sleepefficiency [SE]) and attention and executive functioning in childrenwith ADHD.	Shorter sleep duration was associated with a range of executive functioning problems as reported by the parents ((beta coefficient of .60 for total sleep time for behavioral regulation @ $p<.001$, R squared=.38 and Beta coefficient of .63 for total sleep time for global executive composite score @ $p<.001$, R squared=.29).

Table 1. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations andbiases	Objectives	Summary of main results: Interventions/comparisons/ outcomes
Akinci et al. (2015)	Case control	ADHD: 28, control: 15	71.4%/28.6%	Medication naïve.	8–12 years	PSQI (Pittsburgh Sleep Quality Index), Epworth Sleepiness Scale (ESS), Polysomnography (PSG). Limitations: Small sample size, PSG done for 1 night only.	To evaluate basic sleep architecture and non–rapid eye movement (NREM) sleep alterationsin ADHD children.	Children with ADHD had worse sleep quality (Sleep efficiency, mean, CI, 98.4 (98–98.5) vs. 91.66 (87.16–95.22) @ $p<.001$) and more daytime sleepiness(ESS Score: mean, CI, 1 (0–2) vs. 3 (1.25–5) @ $p<.05$). Polysomnography data showed that the sleep macrostructure was not significantly different however, sleep microstructure was altered in ADHD children by means of reduced total cyclic alternating pattern rate (mean, CI, 61.1 (37.8–66.35) vs. 48.95 (19.25–59.65) $p<.031$) and duration of cyclic alternating pattern sequences (mean, CI, 6 (4.05–7.7) vs. 3.95 (3.2–6.75) $p<.044$).
Andersson and Sonnesen (2018)	Case control	ADHD: 15, control: 36	66.6%/ 33.4%	ADHD children on medication (no details given).	9–12 years	Intra-oral scans, Epworth Sleepiness Scale, Berlin Questionnaire. Limitations: small sample size and some aspects of dental and palatal dimensions could not be measured.	To compare sleepiness, occlusion, dental archand palatal dimensions between children with ADHD and healthy children.	The ADHD children snored significantly more ($p < .05$) and slept restlessly significantly more often compared to the controls ($p < .001$) and had a tendency to sleep fewer hours during the night (<.1) and felt inadequately rested in the morning compared to the controls ($p<.1$).
Scott et al. (2013)	Longitudinal	ADHD: 173, total: 8195	84.4%/ 26.6%	No details given for medication use among ADHD diagnosed children.	6 months-11 years	Subjective created questionnaires for parents, consisting specific questions for sleep and other studied variables. Limitations: missing data and loss to follow-up more likely in socioeconomically deprived groups, psychosocial problems in family not addressed, might be associated with poor sleep and ADHD in children, information on children prescribed stimulant or other medication for their ADHD not reported accurately, subjective (parental reports) measures of sleep patterns and sleep behaviors.	To investigate sleep patterns and trajectories from 6 months after birth to 11 years old, and their relation to ADHD diagnoses.	In children with attention deficit hyperactivity disorder, shorter sleep duration appears early and predate the usual age of clinical diagnosis (at 6 months, mean:10 hour 35 minutes, (SD 1 hour 24 minutes) vs. mean; 10 hour 48 minutes (SD 1 hour 19 minutes) $p=.04$) and (at 6 years 9 months, mean:10 hour 50 minutes, (SD 0 hour 51 minutes) vs. mean; 11 hour 8 minutes (SD 0 hour 40 minutes) $p<.001$) as compared to controls.

(continued)

Table 1. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations andbiases	Objectives	Summary of main results: Interventions/comparisons/ outcomes
Reynaud et al. (2018)	Longitudinal	1342 children (assessed at 2,3,5,6 years)	53%/47%	Not currently medicated.	2–6 years	Strength and difficulties questionnaire. Limitations: measurements for night-waking and inattention/ hyperactivity were both assessedthrough subjective questionnaire measures, lack of statistical power inthe analysis of adjusted associationsbetween covariates and the joint trajectories.	To study the longitudinal associations between inattention/hyperactivity symptoms and night-waking in preschool-years.	Both night-waking and inattention/ hyperactivity trajectories showed persistence of difficulties in preschool years (frequent night-waking trajectories(N = 1076, 80%) and ("rare night-waking"one N = 269, 20%), (high N = 174, 13%), medium (N = 538, 40%) and low (N = 630, 47%) for inattention/hyperactivity z-score trajectories). Additionally, probability of having a high inattention/ hyperactivity trajectory when belongingto the common night-waking trajectorywas of .20, vs. .13 (p = .01) when belonging to the rare one.
Touchette et al. (2009)	Longitudinal	2057 children	68.3%/34.3%	N/A	1.5–5 years	Subjective questionnaires assessing, sleep duration, hyperactivity scores, parental behaviors around sleep periods and potential risk factors, Infant characteristics questionnaire, Diagnostic Interview schedule for parents. Limitations: correlational design does not allow causal inferences, mother's perceptions of her child could have contributed to bias in the findings, most participantswere non-immigrant French-speakingwhites, the findings should be replicated in other populations.	To investigate the developmental trajectories of night-timesleep duration and hyperactivity over the preschool years and to identify the risk factors associated with short nighttime sleep durationand high hyperactivity scores.	Children with low hyperactivity scores are most likely to present an 11-hour persistent night-time sleep-duration trajectory (probability = .36) and children with high hyperactivity scoresare most likely to present a short- persistent night-time sleep-duration trajectory (probability = .35). A $\square^2$ test revealed that night-time sleep- duration and hyperactivity trajectorieswere significantly associated ($\square^2$ = 75.1;p < .001).
Tso et al. (2019)	Longitudinal	514 children	48.5%/51.5%	20 children received stimulant medication (MPH)	5–9 years	Chinese Childhood Sleep Quality Index (adapted from Children's Sleep Habits Questionnaire and the Hong Kong Adolescent Sleep Questionnaire), parent-rated Chinese Strengths and Weaknesses of ADHD-Symptoms and Normal-Behaviors (SWAN) questionnaire. Limitations: children's sleep patterns/quality of sleep based on parental reports rather than objective assessments, presence of ADHD symptoms measured via parent-rated questionnaire (not clinician assessments), some missingdata due to attrition, impaired parent–child relationship may confound the association found, sample size is relatively limited in detecting effect of sex, despite observed effect size difference.	To study prospectively specific sleep patternsand risk of ADHD after adjusting for potential confounders such as obstructive sleep apnea (OSA) and methylphenidate use.	Sleep deprivation in early childhood is associated with higher risk of ADHD in middle childhood (the risk of probable ADHD was 15.5per 100 for children with <8hour of sleep in K3, whereasit was 1.1per 100 for children with 11–12hour of sleep in K3. The adjustedrisk ratio was 14.19 (p = .02) (adjustedfor obstructive sleep apnea and methylphenidate use).

Table 1. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objectives	Summary of main results: Interventions/comparisons/ outcomes
Gregory et al. (2017)	Longitudinal	2042 Childhood ADHD (ADD screened at 5,7,8,10,12 & 18 years)	49%/51%	Participants taking ADHD medication excluded from analysis.	5–18 years	PSQI, ADHD diagnostic tools. Limitations: Self-reports of ADHD and sleep quality may have artificiallyinflated the associations, collected information on sleep quality in young adulthood, but not prior during childhood.	To examine the longitudinal association between ADHD and sleep quality and to explore the genetic and environmental underpinnings of this association.	Children with ADHD had poorer sleep quality in young adulthood (= .19 [95% CIs] = .14, .25, p < .001), but only if their ADHD persisted. Adults with ADHD had more sleep problems than those without ADHD, over and above psychiatric comorbidity and maternal insomnia (hyperactive/impulsive = .13 [95% CIs] = .07, .19, p < .001; inattentive = .20 [95% CIs] = .14, .25, p < .001).
Grünwald and Schlarb (2017)	Cross sectional	ADHD: 72	79.2%/20.8%	Medication naïve.	6 13 years	CSHQ German version, Quality of life questionnaire, parent rated German language questionnaires for diagnosis of ADHD (FBB-HKS). Limitations: Small sample size, gender disparity with more male participants, no objective measurements included.	To examine the links between sleep disorders and subtypes of attention deficit-hyperactivity disorder (ADHD-inattention, ADHD-combined, ADHD-hyperactive/ impulsive) in childhood.	Children with primarily hyperactive impulsive ADHD showed the highest CSHQ-DE scores (parasomnias: ADHD-I, 1.09 (.11); ADHD-H, 1.38 (.31); ADHD-C, 1.26 (.28) (^{2}[2] = 6.343; p = .042) sleep-disordered breathing: ADHD-I, 1.00 (.00), ADHD-H, 1.10 (.16), ADHD-C, 1.17 (.29) (^{2}[2] = 6.107; p = .047) and high impact for insomnia in this subgroup ADHD-I (N = 0; .0%), ADHD-HI (N = 6; 50.00%), and ADHD-C (N = 6; 31.58%) and a high comorbid load for the mutual occurrence of insomnia and nightmares.
Bessey, Coulombe, et al. (2013)	Case control	ADHD: 84, control: 179	Not mentioned	Not mentioned	5–12 years	Sleep Attitudes and Belief Scale (SABS). Limitations: Samples did not significantly differ on most demographic variables, allowing valid between-group comparisons, age of target children were not collected, ADHD/ASD current status of the child could not be determined.	To develop a measure to assess parental beliefs about their child's sleepas a contributing factor for typically developing, ADHD and ASD children.	As compared to the TD children's parents, both ADHD (sleep modifiability subscale: t (352) = –5.60, p < .001; and responsiveness to treatment subscale: t (352) = –2.99, p = .003) and ASD (sleep modifiability subscale: t (352) = –4.27, p < .001, and responsiveness to treatment subscale: t (352) = –3.04, p = .005),children's parent's reported that their child's sleep problems are less modifiable and responsive to change.
Matsuoka et al. (2014)	Case control	Developmental disorders: 43 (out of which ADHD:9), control: 372	90.7%/9.3% (developmental disorders group)	In developmental disorder group, 9 children were on medication (MPH, antipsychotic drugs, antiallergic drugs), in control group 30 on medication (antipsychotic drugs, antiallergic drugs, anti-epileptic).	6–12 years	CSHQ, PSQI. Limitations: Reliability/ validity of used Japanese CSHQ not determined by time of administrationand scoring, medicated children with developmental disorder had higher total CSHQ and sleep onset delay scores than those who were not on medication, suggesting medications may have adverse effects on sleep, only subjective reports of questionnaires used to assess sleep and small female sample.	To analyse the sleep problems of children with developmental disorders, such as pervasive developmental disorder and attention deficit hyperactivity disorder.	The total CSHQ score (r = .429, p < .001), bedtime resistance (r = .376, p < .05),sleep onset delay (r = .372, p < .05), and daytime sleepiness worsened (r = .463, p < .05) with increasing age in children with developmental disorders; in contrast, these parameters were unchanged or became better with age in the control group. In children with developmental disorders, there was a significant association between a higher total CSHQ score and lower academic performance (r = .37, p < .05).

Table 1. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations andbiases	Objectives	Summary of main results: Interventions/comparisons/ outcomes
Noble et al. (2011)	Cross sectional	ADHD: 67	70%/30%	10 children with ADHD were on medication (stimulants or Atomoxetine).	5–12years	Conners Questionnaire, BACS, parenting stress index, impairment rating, CPRS, Child Routines Inventory (CRI)–Parent Report Form, CSHQ. Limitations: Objectivemeasures not used, possibly leading to rater's bias, all aspects of parenting factors not captured,no information about direction of influence between predictor variables and sleep difficulties inchildren.	To examine the extent to which parental influence predicted sleep problems among ADHD children.	Majority of parents/caregivers (73%) reported significant child sleep difficulties. Parental implementation ofdaily routines added to the explained variance in bedtime resistance after considering child and family characteristics (explaining 25% of the variance in CSHQ scores, F (4;62)= 5.21, p<.01).
Sciberras et al. (2017)	Cross sectional	ADHD: 361	75%/25%	268 children with ADHD on medication (stimulants), Melatonin (124), Clonidine (31).	6–12years	CSHQ, Anxiety Disorders Interview schedule, Subjective questions for parents assessing sleep hygiene and parenting consistency and warmth, parental mental health assed through Kessler-6 (K-6). Limitations: Only subjective measures used, no valid measures of sleep hygiene, absence of non ADHD control group.	To examine the association between sleep problemsand parenting and sleephygiene in children withADHD.	Sleep hygiene and parenting are important modifiable factors independently associated with sleep problems in children with ADHD (greater parenting consistency was associatedwith decreased bedtime resistance (R squared =.14) and decreased sleepanxiety (R squared = .08), and with increased delayed sleep onset (R squared = .08) & (poorer sleep hygienewas associated with increased bedtimeresistance (R squared = .14), increaseddaytime sleepiness (R squared = .16), increased sleep duration problems (R squared = .12), and increased delayed sleep onset (R=.08).
Kwon et al. (2014)	Cross sectional	ADHD:56 (with RLS 24, without RLS 32)	91%/9%	All ADHD participants wereon medication.	Mean age 10.7years	Sleep questionnaire and Restless leg syndrome questions. Limitations: Influence of drug therapy not excluded, objective tests such as PSG or iron workup not performed,small sample and absence of a control to compare, comparable number of female participants werenot included in the sample.	To identify the prevalenceof RLS and sleep problems in children with ADHD in Korea.	12.5% had a family history of RLS, 42.9% showed symptoms of RLS, (out of which 3.6% were diagnosed with definite and probable RLS based on sleep questionnaire), 45% of patients had behavioral insomnia, 45% body movements, 30% teeth grinding, 21% kicking legs, unrefreshed sleep 77%, looking tired 50%.

Table 2.2 *Summary of Nine Studies Focussing on Macro-Structural Sleep Properties Among ADHD Children*

Authors/ publication year	Study design	Participant characteristics				Primary measures, limitations and biases	Objective	Summary of main results
		Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age			Interventions/comparisons/outcomes
Lee et al. (2014)	Case control	ADHD: 37, control: 32	100%/0%	Medication naïve.	7–12years	Matching Familiar Figures Test (MFFT) and 72-hour actigraphy. Limitations: Diagnosis was based on interview with no ADHD subtyping, small sample sizes, only male patients.	To examine neurocognitive functions and nocturnal sleep parameters in patients with ADHD, using a cognitive function test andactigraphy.	Patients with ADHD had more sleep problems, including significantly increased sleep latency (mean (SD) 16.2 (19.7) vs. 6.6 (6.2) p=.01), WASO (mean (SD) 57.4 (23.2) vs. 30.7 (13.7) p<.001), and fragmentation index (mean (SD) 16.7 (4.5) vs. 10.3 (4.4) p<.001), and poorer cognitive function(WASO measured by actigraphy positively correlated with the error rate of response measured by the MFFT in the ADHD patient group (rho = .52, p = .012)), compared with controls.
Miano et al. (2019)	Case control	ADHD: 30, control: 27	70%/30%	Medication naïve.	7.5 years-13.5years	K-SADS-PL, NEPSY-II (Neuropsychological Test- Second edition), WISC-V, nocturnal video PSG, actigraphy,Multiple sleep latency test. Limitations: Controls did not undergo actigraphic and MSLT recordings, all childrenunderwent only one PSG recording (first night effect not controlled) and actigraphic recording was performed 1 week before PSG and MSLT,or the week after, depending onthe needs of the child, without checking for naps before PSG recording.	To describe the SWA behavior inthe same group of children with ADHD.	The focus of SWA (Slow Wave Activity) was observed over the centro–parietal–occipital regions in participants with ADHD ((Permutation test, FDR- corrected, p<.01), which remained significant in the subgroups divided between subgroups according to thesleep diagnosis (p<.01).

(continued)

Table 2. (continued)

Authors/ publication year	Study design	Participant characteristics Gender: Sample size and diagnosis	(male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
*Moreauet al. (2013)	Cross sectional	ADHD: 43	58.1%/41.9%	31 children with ADHD on medication (extended and immediate release psychostimulants, Atomoxetine and psychostimulants + Atomoxetine.	6–13years	Conner's Continuous Performance Test (CPT), Actigraph, Sleep diary, CSHQ,Conner's parent rating scale, K-SADS, BRIEF (Behavior Rating Inventory of Executive Functions). Limitations: Small sample size, heterogenous in terms of medication use, half ofsample had inattentive subtypeonly, due to cross-sectional nature, causality between sleep disturbances and daytime functioning measures cannot beinferred.	To investigate potential relationships between two measures of sleep impairments (i.e., sleep duration andsleep efficiency [SE]) and attentionand executive functioning in children with ADHD.	Shorter sleep duration was associated with a range of executive functioningproblems as reported by the parents((beta coefficient of .60 for total sleep time for behavioral regulation @ $p<.001$, R squared=.38 and Betacoefficient of .63 for total sleep time for global executive composite score @ $p<.001$, R squared=.29).
*Aronenet al. (2014)	Case control	CD & ODD: 30(16 comorbid ADHD). Control:30	90%/10%	11 children fromthe clinical group were on medication (Risperidone and MPH)	7–12years	K-SADS, CSHQ, Actigraphy. Limitations: Small sample size,likely limiting the statistical power of the tests used, the actigraphic measurement time (3 nights) was only modest.	To compare the self- and parent-reported sleep problems and objectively measured sleep amount and efficiency in child patients with CD/ ODD and their age- and gender- matched controls.	Children with comorbid ADHD slept significantly less than did the patients with CD/ODD aloneand the controls (total sleep minutes mean±SD=500.3±50.2 (ADHD+CD/ODD) vs. 416.3±59.8 (CD/ODD), $p<.001$ as measuredthrough actigraphy).

(continued)

Table 2. (continued)

Authors/ publication year	Study design	Participant characteristics Gender				Primary measures, limitations and biases	Objective	Summary of main results
		Sample size and diagnosis	(male%/ female%)	Medication use	Age			Interventions/comparisons/outcomes
Wiebe et al. (2013)	Case control	ADHD: 26, Control: 56	62%/ 38%	4 children with ADHD on medication (washout period of 48 hours beforesleep assessment).	7–11years	PSG, actigraphy, Multiple sleep latency test (MSLT), Epworth Sleepiness Scale (ESS). Limitations: Small sample size, pediatric norms not wellestablished for the MSLT, restless legs syndrome was not measured.	To assess the association between habitualsleep patterns and one night of PSG measured sleep with daytime sleepinessin children with ADHD and typically developing children.	Actigraphy measures of sleep restlessness(time awake (r=.48) and activity (r=.48) during the night), as well as time in slow-wave sleep (r=.46), were positively related to mean sleep latencyon the multiple sleep latency test in children with ADHD (@ p<.05).
Bergwerffet al. (2016)	Case control	ADHD: 63, Control: 61	52%/48%	39 children fromthe ADHD group were on medication (stimulants).	6–13years	Actigraphy, CBCL & TRF, SES evaluation on 6-point Likert scale. Limitations: Used objective measure of sleep quality does not provide insight into parent–child interactions.	To gain more insight into sleep problemsin ADHD using objective measuresof sleep quality.	No objectively measured sleep parameters difference was found.
Waldonet al. (2018)	Case control	ADHD: 25, Control: 25	82%/18%	Medication naive.	6–12years	Conners' Parent Rating Scale-Revised: Long Version, Attention Network Test- Interaction (ANT-I), Actigraphy. Limitations: Larger sample size would have allowed more in-depth analysis that may havepermitted analyses examining differences in sex or ADHD presentations.	To examine the relationships between sleep and attention in both typically developing (TD) children and children with ADHD.	Children with ADHD had poorer alerting(689.96 (618.61) vs. 264.60 (341.97), F (1, 48)=9.05, p<.001) and executive attention (1,121.44 (760.68) vs. 483.49 (820.88), F (1, 48)=8.12 p<.01) on the ANT-I and poorer parent-reported attention (71.20 (9.38) vs. 47.64 (10.31), F (1, 48)=71.44, p<.00), poor sleeppredicted performance on alerting attention for children with ADHD and TD children, (R squared=.32, F(1,48)=4.09, Beta coefficient=−4.10, p<.001) whereas the interactionbetween poor sleep and ADHD diagnosis predicted executive attention scores (R squared=.33, F (1, 48)=4.25, Beta coefficient=−5.14, p<001).

(continued)

Table 2. (continued)

Authors/ publication year	Study design	Participant characteristics Gender: Sample size and diagnosis	(male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Poirier and Corkum (2018)	Case control	ADHD: 50, Control: 50	82%/8%	Medication naive.	7–12 years	Actigraphy and sleep diaries for 4 nights. Limitations: Data collected over a number of years, used same method acrossstudies in terms of ADHD diagnosis and actigraphy data collection, it is possible that different results are associated with different presentations of ADHD (sample includedall three subtypes), small sample, larger number of male participants.	To examine the night-to-night variability of sleepbetween typically developing children and children with ADHD.	No night to night variability between theADHD or TD children.
Bessey, Richards,et al. (2013)	Case control	ADHD: 25, Control: 25	88%/12%	Medication naive.	6–12 years	Conners' Rating Scale-R, Demographic Questionnaire,Mini- Motionlogger Actigraphs,Sleep Lab Adaptation Questionnaire (SLAQ). Limitations: Findings should be cautiously generalizedfrom PSG to the home, 1 nightsleep study, small sample, majority male participants in both groups.	To investigate sleeplab adaptation in children with ADHD and typically developing children, using actigraphy and parent–child-completed questionnaires.	ADHD children indeed did not sleep differently than TD children in lab, however sleep efficiency of TD childrenwas more than ADHD children (for TDchildren, sleep efficiency was 79.90% (SD = 10.76%) at home and 86.11% (SD = 7.25%) in the sleep lab; the maineffect (F (1, 48) = 5.79, P = .020) and the interaction were significant (F (1, 48) = 5.53, P = .023).

Table 2.3 *Summary of Sixteen Included Studies Focussing on Micro-Structural Sleep Properties Among ADHD Children*

Authors/ publication year	Study design	Participant characteristics				Primary measures, limitations and biases	Objective	Summary of main results
		Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age			Interventions/comparisons/ outcomes
*Akinci et al. (2015)	Case control	ADHD: 28, Control: 15	71.4%/28.6%	Medication naïve.	8–12 years	PSQI (Pittsburgh Sleep Quality Index), Epworth Sleepiness Scale (ESS), Polysomnography (PSG). Limitations: Small sample size, PSG done for 1 night only.	To evaluate basic sleep architecture and non–rapideye movement (NREM) sleep alterations in ADHD children.	Children with ADHD had worse sleep quality (Sleep efficiency, mean, CI, 98.4 (98–98.5) vs. 91.66 (87.16–95.22) @ $p<.001$) and more daytime sleepiness (ESS Score: mean, CI, 1 (0–2) vs. 3 (1.25–5) @ $p<.05$). Polysomnography data showed that the sleep macrostructure was not significantly different however, sleep microstructure was altered in ADHD children by means of reduced total cyclic alternating pattern rate (mean, CI, 61.1 (37.8–66.35) vs. 48.95 (19.25–59.65) $p<.031$) and duration of cyclic alternating pattern sequences (mean, CI, 6 (4.05–7.7) vs. 3.95 (3.2–6.75) $p<.044$).
Gruber et al. (2009)	Case control	ADHD: 15, Control: 23	66%/34%	Not currently medicated.	7–11 years	CBCL (Child Behavior Checklist), CSHQ & PSG. Limitations: nasal cannulas not used to detect obstructive hypopneas more accurately; and Multiple analyses leading to subsequent potential for type I errors.	To examine sleep architecture and reportedsleep problems in childrenwith ADHD and normal controls.	ADHD group had significantly shorter duration of REM sleep (ADHD-84.18±32.73* vs. TD- 100.23±24.99, $p<.05$).
Díaz-Román et al. (2018)	Case control	ADHD: 20, Control: 20	67%/33%	17 children with ADHD on medication (MPH, Atomoxetine, MPH+Atomoxetine).	7–11 years	Paediatric Daytime sleepiness Scale (PDSS), Paediatric Sleep Questionnaire (PSQ), sleep diary, PSG. Limitations: The impact of possible confounding variables namely, ADHD subtypes, medication, and SCT symptoms were not assessed.	To compare the subjective and objective sleep characteristics of children with ADHD and typically developing children.	No significant difference was found between the groups in almost any objective sleep variable, except forshorter REM latency in the ADHDgroup (ADHD-144.19 (53.53) vs. TD-195.70 (52.75), $p<.01$) and these children showed significantly higher levels of daytime sleepiness (ADHD-10.10 (5.98) vs. TD-5.25 (2.95), $p<.05$) and greater general sleep problems (ADHD-.30 (.17) vs. TD-.11 (.13), $p<.001$) than control children, asreported by their parents.
Grissom et al. (2009)	Case control	ADHD: 13, Control: 16	Not mentioned	Not mentioned	6–10 years	PSG. Limitations: Records from previously conducted PSGs were analyzed, thereby leaving behind possible gaps in full information regarding behavioral and environmental effects for thechild during that time.	To examine eye movements during rapid eye movement (REM) sleep of children with ADHD and a typically developing control group.	The results indicate a pattern of higher amplitude ($U = 44.00$, $p < .01$), lower frequency REM sleep eye movement inchildren with ADHD (with an average rank of 7.62 vs. 21.00 for children with ADHD).

Table 3. (continued)

Authors/ publication		Participant characteristics						Summary of main results
year	Study design	Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Interventions/comparisons/ outcomes
Silvestri et al. (2009)	Case control	ADHD: 55, Control: 20	85%/15%	Not mentioned.	6–12 years	Conners and SNAP-IV Scales, a structured sleep interview and a nocturnal video-PSG. Limitations: PSG was done for only 1 night thereby not controlling the first night's effect in the results.	To examine specific sleep disturbances and sleep disorders in different clinical subsets of ADHD children.	There is a significant difference in almostall the studied sleep variables betweenADHD children and controls (REM% N3%, N2%, SE%, MA INDEX, TST MIN, REM Latency @ $p<.05$) and different sleep disorders seem to address specific ADHD phenotypes (PLMS index- ADHD-I- 9.0 (22.0) vs. ADHD-C-14.5 (19.2) @ $p<.05$) and correlate with severity of symptoms (Restless leg syndrome severity: ADHD-I- 1.3 (5.1) vs. ADHD-C- 6.9 (10.4) @ $p<.05$).
De Dea et al. (2018)	Case control	ADHD: 8, Control: 7	Not mentioned	Medication naïve.	6–10 years	Electroencephalograph(EEG) recordings. Limitations: Smallsample size.	To evaluate the differences between ADHD and healthy children of the power spectral values in delta, theta, alpha, beta and gamma bands, before,during and after sleep spindles.	Results show significant differences concentrated in the period immediatelyafter spindle epochs, in the left hemisphere of the brain, in almost all bands, with greater values in control than in ADHD children (Left Anterior region- $p=.03$; Left central region – $p=.01$; Left posterior region- $p=.04$for the Total values of Delta, Theta, Alpha, Beta & Sigma waves).
Saito et al. (2019)	Case control	ADHD: 21, Control: 18	100%/0%	Sleep inducing medication administered to all ADHD and 2 typically functioning participants.	5–13 years	Raven's Colored Progressive Matrices (RCPM), Das-Naglieri Cognitive Assessment System (DN-CAS), Mogras test (NoruPro Light Systems, Inc., Tokyo, Japan), Continuous Performance Test (CPT), EEG recordings and power spectral analysis. Limitations: No girls in sample, EEG frequency analysis based on one 1-hour recording, frequency analysis in stage 2 maybe different from that of all-nightrecording, medication induced-sleep group included only few individuals.	To evaluate the power of slow sleep spindles during sleep stage 2 to clarify their relationship with executive function, especially attention, in children with ADHD.	Twelve-hertz frontal spindle EEG activitymay have positive associations with sustained attention function (reaction time variability in CPT) ($r=.368$, $p=.0242$).
Ringli et al. (2013)	Case control	ADHD: 9, Control: 9	88%/12%	Within ADHD group: 6 medication naïve, 1 pretreated with MPH, 2 on MPH.	6–12 years	EEG recordings and Power spectral analysis. Limitations: Cross-sectional data with limited age range, which does not offer investigation of intraindividual cortical development or electrical neuronal activity, smallsample size, effect of medicationnot examined.	To compare the sleep EEG of children with ADHD with healthy controls to explore differences in sleep SWA (Slow Wave Activity).	Children with ADHD showed a less mature topographical SWA distributionin comparison to healthy children of the same age and sex. (Calculated Power maps for each group showed that ADHD children exhibited 17% (±6% SE, $p<.01$) more SWA in a cluster of six central electrodes).

(continued)

Table 3. (continued)

Authors/ publication		Participant characteristics						Summary of main results
year	Study design	Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Interventions/comparisons/ outcomes
Miano et al. (2016)	Case control	ADHD: 30, Control: 25	70%/30%	Medication naïve.	8–13 years	K-SADS-PL, NEPSY-II, WISC-V, nocturnal video PSG, actigraphy, Multiple sleep latency test, CSHQ. Limitations: Small samplesize and not comparable numberof female participants.	Full sleep assessment using objective measures for ADHD and control children.	All ADHD children reported a history of sleep problems and slept less than 9 hour per night, indicating chronic sleep deprivation that should be evaluated as a possible unifying marker of ADHD (TST minutes, ADHD- 421.49 (±58.93) vs. Control- 462.8 (±69.57) $p<.022$).
Miano et al. (2019)	Case control	ADHD: 30, Control: 25	70%/30%	Medication naïve.	7.5–13.5 years	K-SADS-PL, NEPSY-II, WISC-V, nocturnal video PSG, actigraphy, Multiple sleep latency test. Limitations: Controls did not undergo actigraphic and MSLT recordings, all children underwent only one PSG recording (first night effect not controlled) andactigraphic recording was performed 1 week before PSG and MSLT, or the week after, depending on the needs of the child, without checking for naps before PSG recording.	To perform a detailed subjective and objective sleep investigation amongADHD children and controls.	Results confirm static and dynamic changes in SWA behavior in childrenwith ADHD, which may reflect a maturational delay occurring at a vulnerable age, as a consequence ofchronic sleep deprivation (In early sleep ADHD children showed a greater amount of delta power overthe centro–parieto–occipital regions (Permutation test, FDR-corrected $p<.01$) In late sleep ADHD children, a greater amount of delta power over the centro–parietal regions were shown (Permutation test, FDRcorrected, $p<.01$).
Přihodová et al. (2012)	Case control	ADHD: 14, Control:12	85%/15%	Medication naïve.	7–12 years	Nocturnal video PSG. Limitations: Scoring of sleep microstructure parameters (arousals) may differ from center to center, small sample size, more male participants.	To evaluate the microstructure of sleep in children with ADHD.	Sleep microstructure analysis using CAP revealed no significant differences between the ADHD group and the controls in any of the parameters under study.
Galland et al. (2010)	Case control	ADHD:27, Control:27	76%/24%	Randomly assigned 48-hour on-off medication protocol was used for ADHD children.	6–12 years	PSG, Behavioral Assessment Scales for Children (BASC), Sleep questionnaire completed by parents. Limitations: Small sample size, majority male participants, sleep debt incurredfor drug use may have caused a rebound effect during washout period, so sleep duration and sleep latency compared on-off medication night could purely be rebound, dosages and formulations of MPH werenot standardized, only one PSG recording was conducted for each condition (on-off medication), so information collected could be subject to afirst-night effect.	To assess the effectsof regular use of methylphenidate medication in children diagnosed with attention deficit hyperactivity disorder (ADHD) on sleeptiming, duration and sleep architecture.	Methylphenidate reduces sleep quantity but does not alter sleep architecture in children diagnosed with ADHD (ADHD children had a significantly longer sleep latency on the medicationnight (65 vs. 38 minutes, $p = .002$), woke earlier in the morning (6:20 am vs. 6:45 am, $p = .03$), with a significantly shorter sleep period time (7.9 hours vs. 9 hours, $p < .001$) and had reducedsleep efficiency (81.7 vs. 87.3, $p < .001$);these medications effects held strongly when control data were taken intoaccount).

(continued)

Table 3. (continued)

Authors/ publication		Participant characteristics						Summary of main results
year	Study design	Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Interventions/comparisons/ outcomes
Galland et al. (2011)	Case control	ADHD: 28, Control: 28	76%/24%	Randomly assigned 48-hour on-off medication protocol was used for ADHD children.	6–12 years	Nocturnal PSG, Sleep and breathing questionnaire. Limitations: Small sample size, majority male participants, parents were not blinded to study/medication status, snoringdata extracted from shortened sleep times on the medication night in children with ADHD, contamination of the PSG data by "first night" effects.	To measure apnea-hypopnea indices and snoring in children diagnosed with ADHD and typically developing controls.	PSG data revealed no significant differences between control group and ADHD children for presence of an AHI >1 or snoring.
Prihodova et al. (2010)	Case control	ADHD: 31, Control :26	83%/17%	Not currently medicated.	6–12 years	PSG (2 nights) and MSLT, CBCL and Conner's Parents rating scale. Limitations: More male participants, ADHD group had ahomogenous make up with morecombined subtype.	To evaluate the microstructure of sleep in children with ADHD.	No REM /Sleep function changes notedin ADHD.
Henriques Filho (2016)	Cross sectional	ADHD: 61	57%/43%	Temporary discontinuation of psycho-stimulant medication before assessment.	8–13 years	PSG and P300 evoked potential test. Limitations: The use of subjectively reported sleep parameters alongside the objective measures, would havegiven a more comprehensive result, keeping in mind the environmental-social-cultural variables at play.	To determine prevalence of OSA in a group of children with ADHD and to compare amplitude and latency of the P300 potential between ADHD children with and without associated OSA.	Significant decreased amplitude of the P300 potential was observed in children with OSA+ADHD when compared with children with only ADHD (without OSA) ($F=3.661$, $p=.028$). The results were confirmed by Spearman correlation analysis, which showed a significant correlationbetween increased AHI and decreasedP300 amplitude (test 1: $r=-.631$, $p=.0001$; test 2: $r=-.672$, $p=.0001$; test 3: $r=.651$. $p=.0001$) in the ADHD+ OSA group).
*Wiebe et al. (2013)	Case control	ADHD: 26, Control: 56	62%/ 38%	4 children with ADHD on medication (washout period of 48 hours before sleep assessment).	7–11 years	PSG, actigraphy, Multiple sleep latency test, Epworth Sleepiness Scale. Limitations: Small sample size, paediatric norms not well established for the MSLT, restless legs syndrome was not measured.	To assess the association between habitual sleep patterns and one night of PSG measured sleep with daytime sleepiness in children with ADHD and typically developing children.	Actigraphy measures of sleep restlessness(time awake ($r=.48$) and activity ($r=.48$) during the night), as well as time in slow-wave sleep ($r=.46$), were positively related to mean sleep latency on the multiple sleep latency test in children with ADHD (@ $p<.05$).

Circadian Rhythms and Chronotype in Attention Deficit Hyperactivity Disorder

Cortisol rhythms

A number of studies have examined diurnal variations in salivary measures for cortisol, which is under strong circadian control as the end product of the hypothalamic-pituitary-adrenal (HPA) axis in children with ADHD and matched control groups of typically functioning children (studies detailed in Table 2.4). Salivary Cortisol awakening response (CAR) was found to be lower in children with ADHD (n = 62) than in controls (n = 40) with a pronounced difference for the ADHD combined presentation (hyperactive and inattentive; Angeli et al., 2018). Contrary to the above finding, a couple of studies revealed no difference in CAR response between ADHD and control groups (Imeraj et al., 2012; Buske-Kirschbaum et al., 2019). Children with ADHD treated with Methylphenidate and with higher morning cortisol levels were found to have better CPT (Continued Performance Test) performance (specifically for impulse control) compared with those with lower levels of the same (n = 50, 6–12 years; Wang et al., 2017). For diurnal cortisol rhythms, children with ADHD compared to typically developing children had significantly lower levels of salivary cortisol at a number of time points during the day (Angeli et al., 2018). Interestingly, Imeraj et al. (2012) showed that for cortisol measures at a number of different time points in a day (waking, noon, 4pm and 8pm) orthogonal contrasts of the overall ADHD group (n = 33, 6–12 years) and the control group (n = 33) did not reveal any group differences, although orthogonal contrasts comparing the ADHD + Oppositional defiant disorder and the ADHD groups revealed significant difference in cortisol measures. In this study specifically, ADHD + ODD subgroup showed significantly higher morning and lower evening levels, resulting in a steeper linear decrease in cortisol levels throughout the day as com- pared to the ADHD subgroup (Imeraj et al., 2012). As a measure of total cortisol output, lower levels of AUCg (area under the curve with respect

to ground) and AUCi (area under the curve with respect to increase) for "wake to bed" period was found in 6 to 10-year-old children with ADHD combined presentation and ADHD-I, suggesting lower overall cortisol secretion over a 24-hour period (Angeli et al., 2018). On the other hand, Buske-Kirschbaum et al. (2019) demonstrated no group differences for AUCg diurnal profiles among ADHD (n = 34, 6–12 years) and control group children.

For stress responses in salivary cortisol, Angeli et al. (2018) showed no statistically significant differences in pre- and post-stress responses (induced through venipuncture) between the ADHD (n = 62) and control group (n = 40). Additionally, these authors did not report different diurnal profiles for the enzyme alpha-amylase for children with ADHD, although after stress response there was an increase in alpha-amylase in the control group but not the ADHD- combined and inattentive groups (Angeli et al., 2018). Buske- Kirschbaum et al. (2019) measured stimulated cortisol secretion (via acute psychosocial stressor elicited by the Trier Social Stress Test), a less pronounced cortisol response was found in the ADHD group (n = 34, 6–12 years) compared to the control group, along with a negative correlation between ADHD symptom score and cortisol stress response (higher the ADHD symptoms, lower the cortisol response).

Cardiovascular rhythms

When considering diurnal profiles for heart rate and activity patterns in children with ADHD, Imeraj et al. (2011) found that heart rate levels were significantly higher in the ADHD group (n = 30) compared to the control group (n = 30), with these group difference particularly expressed during night time and afternoon. In the same study, 24-hour activity patterns measured through actigraphy revealed that between 9 and 10 a.m. and between 11 a.m. and 4 p.m. activity levels were significantly higher in the ADHD group (Imeraj et al., 2011). On similar lines, when seasonal changes in activity profiles were investigated (with two time- point

measurements, T1: December & T2: June) difference between the children with ADHD's levels (n = 10) of nocturnal motor movement in December and in June was greater than that of the control group children (n = 5; Langevin & Ramdé, 2012). In this study, it was found that children with ADHD treated with psychostimulants had higher level of nocturnal motor movements when compared to untreated children with ADHD. With regard to seasonal change in sleep, children with ADHD had significant improvement in sleep quality in T2 as compared to controls.

Melatonin, chronotype, and diurnal activity rhythms

When assessing melatonin rhythms, a study showed that although children with ADHD did not differ from control children in melatonin peaks and maximum night-time levels, their 24-hour melatonin profiles differed significantly, with the duration of the nocturnal melatonin signal shortened in children with ADHD between the ages of 10 and 12 years, due to the significantly earlier morning melatonin decline in the ADHD group (n = 34; Novakova et al., 2011). In another study by Paclt et al. (2011) found no difference in melatonin levels between the 6 to 12-year-old ADHD (n = 4) and control group (n = 43). Tarakçioğlu et al. (2018) investigated chronotype preference among children with ADHD (n = 53) and typically developing (n = 38) children aged 6 to 12 years using the Children's chronotype questionnaire, and revealed no specific morning/evening preference for the ADHD group compared to controls. Van der Heijden et al. (2018) similarly found that chronotype did not differ significantly between groups (ADHD, control and ASD), but evening type was associated with sleep problems in children in the ADHD (n = 44) and TD groups (n = 243). When sleep/activity data was collected at 2 years via actigraphy for 99 pre- term children, and the results were assessed using time series analysis by comparing each child's sleep/activity circadian cycle, it was found that higher toddler activity level was associated with fewer teacher-reported ADHD

symp- toms and a lower risk for illness-related medical visits at 6 years (Schwichtenberg et al., 2016).

Table 2.4 *Summary of Eleven Included Studies Focusing on Circadian Rhythm Markers Among ADHD Children*

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Angeli et al. (2018)	Case control	ADHD: 62, Control: 40	68%/32%	Not currently medicated.	6–10 years	Assessment of salivary samples, Raven's progressive matrices and K-SADS. Limitations: Small sample, diurnal variations assessed for one day, theexact time point of awakening and bedtime was not recorded, stress imposed by venipuncture was not very effective in eliciting stress response of both limbs (stress system and HPA axis).	To assess diurnal rhythms and stress responses in children with ADHD, via consecutive measurementsof specific, extensively used, salivary biomarkers (cortisol for the HPA axis and □-amylase for SNS).	Results revealed that children with ADHD-C had lower mean cortisol values both 30 minutes after awakening (ADHD-C-14.60 (4.43) vs. NoADHD-19.38 (7.10) $p = .002$) and at 18:00 hour than controls (ADHD-C-7.16 (1.93) vs. No ADHD-9.01 (4.18) $p = .018$), as well as lower mean Cortisol Awakening Response (CAR) (ADHD-C-−.40 (4.73), ADHD-I-.56 (8.26) & No ADHD-4.50 (3.97) $p = .001$) and Area Under the Curve for "wake to bed" period (AUCi) values of cortisol (ADHD-C- 1775.88 (693.26), ADHD-I-1868.12 (621.66), No ADHD- 2804.98 (1707.00) $p = .001$), mean CAR and cortisol AUCi were lower in children with ADHD-I than the control group.
Imeraj et al. (2012)	Case control	ADHD: 33, Control:33	82%/18%	28 children took MPH (washout period of 72 hours prior to testing)	6–12 years	Salivary cortisol analysis, CBCL, Level of puberty achieved, BMI, Sleep and wake time (weekend and weekday). Limitations: salivary cortisol collectedin naturalistic environment resulted in some noncompliance, overall small sample, leading to small samplesizes of clinical subgroups (ADHD + ODD and ADHD), subjects with ODD without ADHD not included, activity levels not controlled, no objective test of arousal (i.e., multiplesleep latency test).	To examine across-the-day cortisol variations in ADHD and control children.	Longitudinal analyses to evaluate cortisol profilesacross the day revealed a significant Group · Time effect ($p < .001$), the ADHD subgroup showed a flatter slope with relative morning hypo-arousal and evening hyper arousal, whereas the ADHD + ODD subgroup showed a steeper slope with relative morning hyperarousal and evening hypo-arousal ($p < .001$). Control vs. ADHD (overall) group difference in noon Cortisol levels (showing a large effect size of 0/83 and ADHD + ODD versus ADHD group difference in the evening Cortisol levels (showing a large effect size of .91) however for 4 pm effect size is .25. No
Buske-Kirschbaum et al. (2019)	Case control	ADHD: 34. Remaining sample: 111 (Atopic Eczema- 42, ADHD +Atopic Eczema- 31, controls- 47)	81%/9%	All ADHD children were medication free for more than48 hours prior to testing and all Atopic Eczema patients were anti-inflammatory medication free for 4weeks.	6–12 years	Psychological stress test (TSST-C), SCORAD, Salivary cortisol, FBB-ADHS questionnaire. Limitations: Small sample size, participants with AE to (mild to mild cases, ethics committee requirement), low symptom severity might hindered detection of alterations in HPA axisfunction that would be visible with pronounced AE symptomatology, changes in sleep quantity and quality not assessed, cross- sectional investigation provides onlycorrelational data.	To evaluate HPA axis function, salivary cortisol inresponse to psychosocial stress (Trier Social Stress Test for Children, TSST-C),after awakening (cortisol awakening response, CAR), and throughout the day (short diurnal profile) and hair cortisol capturing long-term HPA axis activity were assessed.	alteration of the cortisol response to the TSST-C was observed in children with AE, however, in children with AE, increased ADHD-like behavior was associated with a reduced HPA axis response to acute stress (for children with AE (with or without an additional diagnosis of ADHD), Impulsivity, Inattention, and Total scores were negatively correlated with the percent change in salivary cortisol in response to the TSST-C (effect sizes $r = -.21$, $p = .031$, $r = -.29$, $p = .004$, and $r = -.23$, $p = .020$, respectively). Groups did not differ in CAR,short diurnal profile, and hair cortisol.

(continued)

Table 4. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations andbiases	Objective	Summary of main results: Interventions/comparisons/outcomes
Wang et al. (2017)	Case control	ADHD: 50, Control: 50	80%/20%	Not currently medicated.	6–12 years	SNAP-IV, CBCL, CPT, ADHD-RT, Saliva Cortisol test. Limitations: Saliva samples collected from patients in hospital but from healthycontrols in school, no measurementsof cortisol increment levels were made after baseline and during first month of treatment, waking time of participants was not precisely identified, patients with ODD or conduct disorder excluded.	To determine the trend in cortisol levels in children with ADHD and controls.	The cortisol levels of ADHD patients increased significantly after 1 month of MPH treatment (significantly higher than those at pre- treatment; mean difference = .11, $p = .046$). before decreasing to an intermediate level, but were significantly positively correlated with neuropsychological performance (salivaryCortisol was found to be independently and significantly correlated with impulse control (=−.006, $p = .003$).
Imeraj et al. (2011)	Case control	ADHD: 30, Control: 30	80%/20%	Not currently medicated.	6–11 years	Actigraph, Actiheart, CBCL, Demographic variables. Limitations: higher stress levels expected to elevate heart rate levels, so that differential results in ADHD may bedue to secondary conditions rather than to ADHD itself, pubertal stage/sex/stimulant medication/caffeine use/presence of nightmares/regular physical training.	To investigate 24-hour heart rate patterns under natural environmental conditions among ADHD and control children.	Heart rate levels were overall higher in the ADHD group ($p < .01$)—with the largest effects during afternoon (effect size- .69) and night (effect size – .57) ($p<.001$)—in a modelcontrolling for age and children with ADHD showed higher activity levels during daytime (especially early afternoon) (effect size – .83)($p< .05$), but not during night-time (effect size- .11).
Langevin and Ramdé (2012)	Case control	ADHD: 10, Control: 5	80%/20%	5 children with ADHD on psychostimulant medication.	7–9 years	Sleep log, Actimetry, French version (SWAN-F). Limitations: All data from Actiware not assessed, time ofstudy coincided with week before Christmas holidays, leading to differences in excitement level of children (particularly ADHD), small sample size.	To verify that the shortening photoperiods of winter contribute to increasing the nocturnal and diurnal agitation of children with ADHD and that lengthening photoperiods diminish it.	Results show a significant baseline difference between the nocturnal motor movements of the ADHD children (on and off psychostimulants) and those of the control children ($p = .008$) during the winter peak (December). The same was also true for diurnal agitation (inattention, hyperactivity) between the ADHD (not on psychostimulants)and control group ($p = .008$) for both the winter (December) and summer (June) time points.
Novakova et al. (2011)	Case control	ADHD: 34, Control: 43	70%/30%	Not currently medicated.	6–12 years	Saliva specimens were collected in four different sessions around the time of the spring and autumn equinoxeswhen the natural light lasted 11.2 ± .9 hour. Limitations: Small sample, majority male participants.	To examine the salivary Melatonin rhythms among children with ADHD and controls.	Age based categorization of children, revealed significant differences between the ADHD and control group in the melatonin rhythm waveform (when the profiles of the 6–7-year-old and 10–12 year-old ADHD and control children were compared, significant differencesin melatonin values between these ages at 22:00hour ($p <.001$) and 06:00hour ($p = .001$),suggesting that the entire profile in the older children was phase delayed relative to the younger children.

(continued)

Table 4. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Paclt et al. (2011)	Case control	ADHD: 34, Control: 43, Anxiety: 11	Not mentioned	Not currently medicated.	6–12 years	Saliva specimens were collected in four different sessions during the school year, around the time of the spring and autumn equinox, when the natural light lasted 11.2 hour ± .9 hour. Limitations: Small sample size.	To examine salivary Melatonin levels during Spring and Autumn equinoxes among ADHD, controls and Anxious children.	More symptoms of conduct disorder elevated positive or negative correlations between psychopathology and saliva level of melatoninin ADHD and anxiety samples (for example ADHD children exhibit positive correlation ($p <$ .01), correlation of .438 between the melatonin level at 18 hours and hyperactivityscore at Conner's scale and correlation (p<.01), .541 for conduct disorder score in Conner's scale).
Tarakçioğlu et al. (2018)	Case control	ADHD: 53, Control: 38	81%/19%	Not currently medicated.	6–12 years	CSHQ, Childhood Chronotype Questionnaire (CCTQ). Limitations: small sample size, Turkish version of CCTQ not enough sensitivity and specificity to assess preferencesof morningness and eveningness, in both groups, almost all parents reported eveningness type, only subjectively assessed parental reportsused, comorbid psychiatric concerns not analyzed statistically due to inadequate number of comorbid cases.	To investigate the relationship between circadian characteristics and behavioral problems inchildren with ADHD and controls.	ADHD children had more sleep-onset problems (Bedtime resistance- ADHD: 12.5 (2.5) vs. Control: 11(3.2) @ p<.023) and parasomnias – ADHD: 9.5 (2) vs. Control: 8.2 (1.5) @ p < .003) compared to healthy controls and circadian preferences did not differ between the groups in CCTQ scores.
Van der Heijden et al. (2018)	Case control	ADHD:12 (within psychiatric group: 112), Control: 271	70%/30%	16% of children with ADHD were on Melatonin and 79% of children with ADHD were on MPH.	6–12 years	CCTQ, CSHQ, Childhood Sleep Disturbance Scale (CSDS), CBCL (Child Behavior Checklist), Parent questionnaire for Sleep onset latency (SOL), Electronic Media use rating scale. Limitations: Assessments basedon subjective parent reports (use of objective measures ex. actigraphy ordim light melatonin onset would havestrengthened results), for etiological role of sleep hygiene and chronotypelong term cohort studies required, influence of medication.	To understand the association of sleep patterns with sleep hygiene among children with ADHD, ASD and typically developing (TD) controls.	Chronotype did not differ significantly between groups, but evening types were associated withsleep problems in ADHD (□ = .471, p = .002)and TD (□ = .317, p < .001) and more sleep problems were shown in ADHD than TD (Disorders of initiating and maintaining sleep @ p<.001, sleep-wake transition disorders @ p<.001, disorders of excessive somnolence @ p<.001, sleep hyperhidrosis@ p<.01, totalsleep problem score @ p<.001).
Schwichtenberg et al. (2016)	Longitudinal	99	53%/47%	Not currently medicated.	2–6 years	Infant prematurity and medical risk records, CBCL, Conner's questionnaires, Actigraph (micromini motion logger), Abbreviated BatteryIQ (ABIQ), Illness related health care visit records. Limitations: TSA framework did not provide a model of daytime napping or a midday dropin activity, large and non-random attrition from 3 to 6 years (mostly non-caucasian), thereby limiting generalizibility, bidirectional nature of sleep and developmental/health concerns not focused on.	To assess the associations between toddler circadian sleep/activity patterns and later developmental, behavioral, attentional, and health concerns in this at- risk population.	Toddlers with patterns that closely aligned with the specified 24-hour circadian cycle (SCC) had higher abbreviated intelligence quotient scores at 3 years of age (beta coefficient of .235 for the closest fit to prototypical circadianpattern and cognitive skills (ABIQ scores) at age 3 @ p< .05), at 6 years had lower risk for illness-related medical visits (incidence rate ratio (IRR) of .749 for the closest fit to prototypical circadian pattern and child illness related health care (total medical attention) atage 6 @ p<.001).

Functional Consequences of Sleep Functioning in Children with ADHD

Behavioral consequences

Emotional and behavioral problems may contribute to sleep problems in ADHD and may also exacerbate negative impacts of disturbed sleep in children with ADHD (relevant studies detailed in Table 2.5). It is reported that anxiety ratings in children aged 7 to 13 years with ADHD (n = 181) were associated with bedtime resistance and sleep anxiety, whereas depressive symptoms were associated with shorter sleep duration and increased day time sleepiness, along with a unique association of oppositional defiant symptoms with shorter sleep duration; further girls with ADHD had more sleep problems and greater anxiety than boys (Becker, Froehlich, et al., 2016). As such, anxiety and/or depression exacerbated total sleep problems and further interacted with ADHD symptoms to predict sleep length and sleep duration problems (Tong et al., 2018, ADHD symptoms n = 82, 9–12 years). Similarly, teacher reported daytime sleepiness in 5 to 13-year- old children with ADHD was associated with higher levels of emotional and behavioral problems in the classroom (n = 257, Lucas et al., 2019). Poorer caregiver reported well-being (behavioral and emotional problems) in similarly aged children with ADHD (n = 186) was associated with transient or persistent sleep problems (Lycett et al., 2016). Further, sleep problems in ADHD are positively correlated with parent-reported perfectionism, psycho- somatic complaints and anxious thoughts (Blunden et al., 2011, n = 88) and predicted adolescent irritability (Mulraney et al., 2017, n = 140). Children with ADHD and internalizing comorbidities had higher reported sleep anxiety than children with ADHD alone (Lycett, Sciberras, et al., 2015, n = 392). Mulraney et al. (2016) found that although there is a weak evidence of a bidirectional relationship between sleep problems and emotional problems in 270 children with ADHD (stable over a 12-month period among age of 5–13 years), they did not appear to influence each other after the 12-month period.

A longitudinal study (n = 3,800) exploring the relation- ship between sleep and the presence of pre-teen delinquency in relation to ADHD symptomatology and diagnosis revealed that sleep problems during childhood were significantly associated with higher odds of ADHD symptomatology, receiving a ADHD diagnosis and pre-teen delinquency (ORs of 2.38–8.10; Jackson & Vaughn, 2017). However, the association between sleep problems and pre-teen delinquency was no longer significant once ADHD symptomatology and diagnosis were considered (Jackson & Vaughn, 2017). In a study exploring the effects of circadian and behavioral tendencies on sleep onset problems for children with ADHD, it was found that for both the 7 to 11 years aged clinical (n = 26) and control (n = 49) group participants' externalizing problems yielded significant independent negatively correlated with verbal IQ (WISC-III) and predicted response latency time in an evaluation of cognitive reflection-impulsivity. In another study (n = 56, 6–12 years), actigraphy-measured bed time movements predicted poorer performance on the cognitive assessment subscales of vocabulary and similarities (WISC-III subtests for assessing retrieval of learned verbal information and abstract reasoning/concept formation respectively) and general memory index score (assessing immediate and short term verbal memory) on a standardized memory and learning test (Suratt et al., 2011). Zambrano-sánchez et al. (2013) found correlation between the presence of specific sleep disorders and WISC-IV measurements among 7 to 12 year old children with individual subtypes of ADHD (n = 156); children with ADHD-combined presentation showed significant correlations between periodic limb movements during sleep and coding subtest value (measuring processing speed), between obstructive sleep apnea-hypopnea syndrome and block design values (measuring Perceptual reasoning) and between inadequate sleep hygiene and digit span subtest values (measuring working memory), whereas children with ADHD-Hyperactivity showed significant correlations between sleep apnea and digit space score and inadequate sleep hygiene and block design scores; and finally, children with ADHD-Inattentive

showed significant correlations between inadequate sleep hygiene and each of coding, block designs, and digits span scores (Zambrano Sanchez et al., 2013). A prospective study (birth to 8.5 years, n = 1120) found persistent regulatory problems in sleep behaviors during infancy predicted lower IQ, increased attention deficits as observed during the test situation, and considerably increased odds of an ADHD diagnosis during preschool years (Schmid & Wolke,2014).

When assessing procedural learning through motor sequence task (MST) in childhood ADHD (10–12 years), an association was found between slow spindle sleep EEG frequency activity and overnight improvement in MST precision; specifically, MST precision was positively associated with slow spindle activity for the ADHD group (n = 7) but not for TD group (n = 14) (Saletin et al., 2017). Similarly, another study found that sleep-associated improvements in reaction times in a motor skills task were positively correlated with the amount of sleep stage 4 and REM-density in children with ADHD (n-16) but not in the control group (n- 16), suggesting that sleep in ADHD normalizes deficits in daytime procedural memory (Prehn-Kristensen et al., 2011). Prehn-Kristensen et al. (2017) found that in a task of rating faces for emotional content, pupilometry and behavioral data revealed among 8 to 11-year-old children with ADHD and comorbid ODD (n = 16) performance did not improve after sleep, unlike the post-sleep improvement noted in the matched controls (n = 16). For consolidation of behavior learned by probabilistic reward, it was found that 8 to 12-year-old children with ADHD (n = 7) do not show sleep-dependent consolidation of rewarded behavior, whereas typically functioning children (n = 17) consolidate rewarded behavior better during a night of sleep, and the level of consolidation correlates with non-REM sleep (Weisner et al., 2017).

Independent from the studies discussed in this review, a typically developing primary school child, in a 24- hour cycle needs about 12 hours of sleep per night and nearing 9 hours

of sleep thereafter (Spruyt & Gozal, 2010). Again, discussing the impact of sleep restrictions, children between the age of 10-14 years with 5 hours of restricted sleep can demonstrate impaired cognitive performance (verbal creativity and memory related sorting task) (Randazzo et al 1998), whereas those with 1 hour more sleep faired better in continuous performance tasks (Sadeh et al 2003). A child showing more sleepiness over a longitudinal period was found on the other hand to have slower improvement in verbal comprehension tasks over a period of 3 years (Bub et al 2011). The above discussed associations between sleep related difficulties and impaired cognitive functions are therefore not only limited to neurodiverse children.

Lifestyle factors and sleep in ADHD

Yürümez and Kılıç (2016) reported that pediatric quality of life scores in 7 to 13-year-old children with ADHD (n-=46) with sleep problems were significantly lower than control group children (n = 31), with ADHD children receiving worse parent ratings in the scale's Psychosocial subscale. The relationship between sleep-related problems and dietary intake in children with ADHD (n = 88, 6–13 years) has been examined, with higher consumption of fats (mono- and polyunsaturated), energy, carbohydrates and sugar being positively associated with sleep disturbances (Blunden et al., 2011). Moreover, ADHD has been associated with lower adherence to a diet of fish, pulses, pasta or rice and a significant difference between ADHD (n = 41, 6–12 years) and controls group (n = 48) for sedentary behaviors and sleep quality (by assessing hours of sleep on weekdays and weekends) (San Mauro Martín et al., 2018). Further, an increased risk of obesity in children with ADHD symptoms (n = 82, 9–13 years) was found to be associated with overuse of electronic devices, eating while using electronic devices, and delaying bedtimes to snack and use electronic devices (Tong et al., 2016). Considering screen time, children with more ADHD symptoms (n = 82, 9–12 years) and screen time before bedtime tended to have shorter sleep times on week- ends (Tong et al., 2018). A longitudinal study (n = 817) where parent rated sleep, TV watching, physical activity and engaging in cognitively stimulating activities at 4 years and ADHD screener and behavioral questionnaire at 7 years was investigated among a cohort, found that shorter sleep duration and less time spent in cognitively stimulating activities were associated with increased risk of developing ADHD symptoms and behavioral problems (Peralta et al., 2018).

Table 2.5 *Summary of Thirty-Four Included Studies Focussing on Consequences of Sleep Functioning in Children with ADHD*

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Becker et al. (2018)	Cross sectional	ADHD: 181	86%/14%	Not currently medicated.	7–13 years	CSHQ, Vanderbilt ADHD Diagnostic Parent Rating Scale (VADPRS), Revised Child Anxiety and Depression Scales, Parent Version (RCADS-P). Limitations: Cross-sectional study cannot indicate causality, few children in sample met criteria for comorbid diagnoses thereby limiting generalizability, sole reliance on parent-reported rating scales which may have contributed to mono-informant biases.	To examine gender based differences in sleep functioning among ADHD children.	Specific ADHD subtypes associated with specific sleep concerns (for example sleep onset delay $r = .15$ @ $p < .05$ level; sleep duration $r = .17$ @ $p < .01$ level; night wakenings $r = .24$ @ $p < .01$ level and parasomnias $r = .26$ @ $p < .001$ level associatedwith ADHD- Hyperactivity/ Impulsivity) and girls had poorer sleep functioning than boys across most sleep functioning domains (75%of girls ($n = 42$) met the establishedcut-off for having sleep problems, compared to 53% of boys ($n = 66$), total sleep disturbance, sex based difference Effect Size: Cohen's $d = .58$)).
Lucas et al. (2019)	Cross sectional	ADHD: 257	74%/26%	201 children with ADHD were on stimulant medication.	5–13 years	CSHQ, Teacher's Daytime Sleepiness Questionnaire, Strengthand Difficulties Questionnaire (SDQ). Limitations: cross-sectionaldesign (no focus on additional predictive factors, beyond target variables), average study sample were taking ADHD medication; thus not clear whether results would generalize to less impaired sample of patients.	To determine if sleep problems and daytime sleepiness were associated with the social, emotional, and behavioral school-basedfunctioning of children with ADHD.	CSHQ subscale night waking was correlated with teacher-rated daytime sleepiness ($r = .25$ @ $p < .001$) and this in turn was associated with higher levels of emotional (= .36; 95% CI = .24–.49, R squared = .25) and behavioral problems (= .51; 95% CI = .40–.62, R squared = .37).
Lycett et al. (2016)	Cross sectional	ADHD: 186	86%/14%	143 children with ADHD were on medication (short and long acting MPH, Dexamphetamine, Atomoxetine).	5–13 years	CSHQ, Paediatric Quality of Life Inventory. Limitations: Child/family well-being already markedly worse for children experiencing transient/persistentsleep problems, study could further explore long term followup format to delineate this relationship.	To examine the longitudinal relationship between sleep problem trajectories and well-being in children with ADHD.	Children with either transient (95%confidence interval (CI) .4, 1.0; $p < .001$) or persistent sleep problems (95% CI, .2–1.2; $p = .004$) had greater (7 standard deviationunits higher) caregiver-reported conduct and emotional problemsover the 12-month period.
Blunden et al. (2011)	Cross sectional	ADHD: 88	78%/22%	Not currently medicated.	6–13 years	Victorian Cancer Council food frequency questionnaire (FFQ), Sleep Disturbance Scale for Children (SDSC). Limitations: No measure for preservatives and additives contained in foods/drinks, no control group and no randomized design (difficult to ascertain any causal pathway), self-selected sample, sleep-dietary intake subjectively assessed by parental reports, psychosocial factors not measured.	To investigate relationships between sleep and dietary macronutrient intake in children with ADHD.	Parents who reported more sleep disturbance also reported a higher intake of carbohydrate: ($r = .26$, $p < .05$), poly fats ($r = .25$, $p < .05$), and, most particularly, sugar ($r = .30$, $p < .01$) which was also a significant predictor of night time sweating (beta coefficient of .261, $p = .018$, R Squared = .22).

(continued)

Table 5. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Mulraney et al. (2017)	Longitudinal study	ADHD:140	89%/11%	139 children with ADHD were on medication.	5–13 years	Disorders of initiating and maintaining sleep (DIMS) subscale from the Sleep Disturbance Scale for Children (SDSC), Strengths and Difficulty questionnaire, ADHD-RS-IV, Affective ReactivityIndex (ARI), Depression Anxiety Stress Scale (DASS-21) for parents, Socio-Economic Indexes for Areas (SEIFA) Disadvantage Index. Limitations: no assessmentof irritability at baseline, 35% of original sample participated in follow-up which may limit the generalizability of results, only 15 girls in sample (results cannot be generalized to girls).	To study if internalizing and externalizing problems predict adolescent irritability 3 years later and if child (behavior, sleep, school attendance) and parent factors (parental mental health) are associated with adolescent irritability.	Irritability was associated with increased attention-deficit/ hyperactivity disorder symptom severity (parent-report (=.45; 95% CI=[.30, –.60]; $p<.001$) and teacher-report (=.33; 95% CI=[.16, –.49]; $p<.001$) and sleep problems (=.28;95% CI =[.12, –.45]; $p=.001$); poorer emotional (=.47; 95% CI=[.30, –.64]; $p<.001$), behavioral (=.64; 95% CI=[.54, –.74]; $p<.001$) and social functioning (=.44; 95% CI=[.28, –.61]; $p<.001$); and poorerparent mental health (=.33; 95% CI=[.22, –.53]; $p<.001$, stress level).
*Lycett, Sciberras, et al. (2015)	Cross sectional	ADHD: 392	85%/15%	333 children with ADHD were on medication (Psycho stimulants and Atomoxetine)	5–13 years	7-day sleep log, CSHQ, ADHD-RS-IV, sleep problems severity assessment, Depression anxiety stress scale, Anxiety Disorders Schedule for Children-IV, Socio-Economic Indexes for Areas. Limitations: All sleep measure's reliance on parental report reflect common effect of parentalperception across the measures, findings limited to behavioral sleep problems, two-thirds of parents returned the sleep log, which may have under- or over-ascertained problem sleepers.	To examine the association between sleep problems and internalizing and externalizing comorbidities in children with ADHD.	Compared to children without comorbidities, children with co-occurring internalizing and externalizing comorbidities were more likely to have moderate/ severe sleep problems (adjusted OR2.4, 95% CI 1.2; 4.5, $p=.009$) and problematic sleep across six of seven sleep domains (bedtime resistance, Sleep duration, parasomnias, night waking, daytime sleepiness, sleep anxiety and total sleep problems).
Mulraney et al. (2016)	Cohort study	ADHD:270	85%/15%	214 children with ADHD were on medication (details not mentioned)	5–13 years	Strengths and Difficulty questionnaire, ADHD-RS-IV, CSHQ. Limitations: Reliance on caregiver report (sleep and internalizing/externalizing problems), CSHQ does not adequately capture sleep- onset latency or sleep qualitywhich objective measures (eg, actigraphy) might ideally assess, study design does not examine longitudinal relationship betweenvariables.	To investigate the bidirectional relationship between sleep problemsand internalizing/ externalizing problems.	Sleep problems at baseline predicted emotional problems at 6 months($r=.17$, $p<.01$), and emotional problems at baseline predicted sleep problems at 6 months ($r=.07$, $p<.05$)and the relationship between these two variables was stable over time (12 months).

Table 5. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Gruber, Fontil,et al. (2012)	Case control	ADHD:26, Control:49	65%/35%	9 children with ADHD were on medication (MPH, Atomoxetine)	7–11 years	CBCL, CSHQ, PSG, Child morning-evening preference scale (CMEP), Child morning-evening preference scale (CMEP). Limitations: Participants below cut-off score on Pediatric Sleep Questionnaire (sleep disordered breathing not assessed objectively) objective circadian measures, ex. salivary melatonin/core body temperaturenot used, one-third ADHD children prescribed stimulants to control symptoms had potentiallyshort wash-out periods (transientworsening of symptom might occurred after medication was stopped).	To determine the relative contributions of circadian preferences and behavioral problemsto sleep onset problemsin children with ADHD.	Externalizing problems yielded independent contributions to parental reports of bedtime resistance (beta coefficient of .90 for the CBCL externalizing T-score and bedtime resistance @ $p<.05$, R squared = .10), whereas an evening circadian tendency contributed to parental reports of sleep onsetdelay (beta coefficient of .37 for Eveningness -score and CSHQ sleep onset delay @ $p<.01$, R squared = .20) and PSG-measured sleep-onset latency (beta coefficientof 8.16 for Eveningness -score and PSG sleep onset delay @ $p<.01$, R squared = .16).
Thomas et al. (2018)	Cross sectional	ADHD: 392 (out of which ADHD+ASD:93, ADHD:299)	85%/15%	Within ADHD group 255 were on medication and within ADHD+ASD group 78 were on medication for ADHD symptoms.	5–13 years	Anxiety Disorders Interview Schedule of Children IV/Parent version (ADIS-C), CSHQ, Peer problem subscale of the Strengthsand Difficulties Questionnaire (SDQ). Limitations: Reliance on parent report of ASD diagnosis, rather than clinical interview, reliance on parent report of behavioral sleep problems, no data for children taking medication for sleep problems, ex. melatonin, which could have influenced results.	To examine the types and severity of behavioral sleep problems experienced by children with comorbid ADHD + ASD compared with those with ADHD.	Children with ADHD + ASD experienced similar levels and types of behavioral sleep problems compared with those with ADHD (Effect sizes ranged from −.05 to .12, indicating very small differences between the two groups) and co-occurring internalizing and externalizing comorbidities was associated with sleep problems in thisgroup (□ =.19).
Soehner et al. (2019)	Longitudinal	ADHD: 145 (among, High risk youth:267 Community comparison control group:217)	50.6%/49.4%	56 participants from the entire group were on Stimulant/non stimulant ADHD medicationand 60 were on Antipsychotic, antidepressant, mood stabilizer and sedative/ hypnotic medication.	10–18 years	School Sleep Habits Survey (SSHS), KSADS-PL, Child Affective Lability Scale (CALS), Screen for Child Anxiety Related Emotional Disorders (SCARED), Disruptive Behavior Disorders Rating Scale. (DBDRS). Limitations: Identified longitudinal sleep-psychopathology associations,but causal interpretations cannot be made, missing data,sleep assessed via self-report; accurate report of sleep patternscan be affected by presence of psychiatric symptoms, objective, youth-report, and parent-report measures would be more accurate.	To identify sleep patterns that longitudinally changein conjunction with psychiatric symptom severity in at-risk youth.	Sleep predictors accounted for 33.1%of the explained variance (5.3% total variance) in the multivariate psychiatric symptom outcome.

(continued)

Table 5. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
*Moreau et al. (2013)	Cross sectional	ADHD:43	58.1%/41.9%	31 children with ADHD on medication (extended and immediate release psychostimulants, Atomoxetine and psychostimulants + Atomoxetine.	6–13 years	Conner's Continuous Performance Test (CPT), BRIEF (Behavior Rating Inventory of Executive Functions), Actigraph, Sleep diary, CSHQ, Conner's parent rating scale, K-SADS. Limitations: Small sample size, heterogenous in terms of medication use, half of sample had inattentive subtype only, due to cross-sectional nature, causality between sleep disturbances and daytime functioning measures cannot be inferred.	To investigate potential relationships between two measures of sleep impairments (i.e., sleep duration and sleep efficiency [SE]) and attention and executive functioning in children with ADHD.	Shorter sleep duration was associated with a range of executive functioningproblems as reported by the parents((Beta coefficient of .60 for total sleep time for behavioral regulation @ p <.001, R squared=.38 and Beta coefficient of .63 for total sleep time for global executive composite score@ p< .001, R squared=.29 from the BRIEF rating scale).
Kidwell et al. (2017)	Longitudinal	271 children	50.6%/49.4%	Not mentioned.	3–11 years	Sleep problems subscale of the Child Behavior Checklist (CBCL), CSHQ, Executive control battery, Conner's teacher's rating scale. Limitations: Sleep assessed at age 3 limited by parent-report format, ADHD symptoms may not be well-measured in 3-year-olds as in older children, ADHD symptoms assessed in community sample (teacher-report), sample primarily European American, which is regionally representative of the Midwest of United States.	To examine longitudinal associations among sleep, executive control,ADHD symptoms in children.	Sleep problems and executive control deficits early in development were associated with increased risk for ADHD symptoms in elementary school. Those with both sleep problems and EC deficits experienceda trend toward more inattention symptoms, (b=−16.88, SE= 8.89, p = .058). Those with both sleep problems and EC deficits experiencemore hyperactivity symptoms than those with high EC, (b=−18.59, SE=9.11, p=.041).
Cremone, Kurdziel, et al. (2017)	Case control	ADHD:18, Control:15	72%/28%	2 children with ADHD were on medication (abstained from medication for 48hours prior to testing)	4–8years	PSG, Go/No-Go task to assess inhibitory control and sustained attention, Diagnostic Interview Schedule for children-IV. Limitations: Small sample size, more male participants.	To examine sleep microstructure in ADHD and typically developing children and its effect on executive functions.	Inhibitory control/sustained attention was not improved following overnightsleep in ADHD children although REM theta activity was greater in children with ADHD. Theta activity recorded during REM was significantlygreater in the ADHD group compared to the TD group (p=.014).Region specific differences in theta activity between ADHD and controlsshowed greater activity in the frontal(p = .038) and central (p = .081) electrode locations for the ADHD group. Unlike, the control group, for ADHD group, neither scores for inhibitory control (p = .38) nor sustained attention (p=.48) changed compared to baseline after sleep in the morning.

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Table 5. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Sciberras et al. (2015)	Cross sectional	ADHD:189	85%/15%	149 children with ADHD were on medication.	5–13 years	Working Memory Test Battery for Children (WMTB-C), CSHQ, Sleep self-report (SSR), Diagnostic Interview Schedule for children-IV, Socioeconomic Indexes for Area (SEIFA). Limitations: Reliance on subjective report measures, rather than objective, assessmentof broad range sleep problems over past week, rather than specific difficulties on night before assessment, severe sleep problems in sample may have limited study's ability to detect relationships between sleep and working memory, majority children with ADHD onmedication, might have influencedresults.	To examine the relationship between sleep problems and working memory in children with ADHD.	As stated in the findings for each standard deviation increase in parent-reported bedtime resistanceproblems, working memory scores decreased by 3.4 points (95% CI: −6.3, −.6; p = .02), also for each standard deviation increase in child-reported sleep problems, working memory scores decreasedby −4.2 points (95% CI: −7.0, −1.4; p = .004).
Cremone et al. (2018)	Case control	ADHD:18, Control:15	72%/28%	2 children with ADHD were on medication (abstained from medication for 48 hours prior to testing)	4–8 years	Diagnostic Interview Schedule for children-IV, Dot Probe task. Limitations: No sleep measure used in this study, although the effect of before and after sleep onthe dot probe task was studied, no social-emotional tool used to measure individual differences that might affect reactions ADHDvs. the control children, small sample.	To determine whether emotional attention biases are evident in young children with clinically significant ADHD symptoms.	ADHD children had significant attention biases toward positive stimuli (happy faces shown in the dot probe task) (p = .027) whereas typically developing children had no significant attention bias for positivestimuli, (p = .130). Also positive attention bias was significantly greaterin ADHD children as compared to typically developing children(p = .008).
*Saito et al. (2019)	Case control (ADHD	ADHD:21(ADHD+ASD-10), Control:18	100%/0% group) 50%/50% (Typically developing group) 75%/25% (ADHD+ASD) .	ADHD children were ADHD medication naïve, however before the testing sleep sessions all ADHD patients and 2 typically developing children were administered pentobarbital (1.25–2.5 mg/kg wtor triclofos sodium(50–70 mg/kg wt).	7–12 years	Raven's Coloured Progressive Matrices (RCPM), Das-Naglieri Cognitive Assessment System (DN-CAS) and Mogras test with the Continuous Performance Test(CPT), Electroencaphalography (EEG), Swanson, Nolan, and Pelham IV scale (SNAP-IV), Parent-interview ASD Rating Scale (PARS-TR). Limitations: No girls in sample, EEG frequency analysis based on one 1-hour recording, frequency analysis in stage 2 may be different from thatof all-night recording, medicationinduced-sleep group included onlyfew individuals.	To evaluate the power of slow sleep spindles during sleep stage 2 to clarify their relationship with executive function,especially with attention,in children with ADHD and controls.	The relative power at 12 Hz was significantly higher in the ADHD + ASD compared to the TDC group at the frontal regions, additionally, the relative power at 12 Hz was significantly higher in theADHD + ASD compared to the ADHD group (p < .01) and there was a significant correlation between the ratio of 12-Hz spindles and reactiontime variability on CPT (r = .368, p = .0242).

(continued)

Table 5. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Surratt et al. (2011)	Cross sectional	Edonotonsillar Hypertrophy: 56	47%/53%	Not currently medicated.	6–12 years	Actigraph, PSG, Subscales from the WISC-III, Wide Range Assessment of Memory and Learning (WRAML), Conner's Continuous Performance Test (CPT), Connor's Parent Behavior Rating Scale long form. Limitations: PSG the night after cognitive testing does not describe child's sleep night before testing, used visual inspection of actigraph graph in conjunction with the sleep diary to determineTime in Bed since no published criteria for children with sleep apnea.	To determine whether frequent movements over six nights during Time in Bed detected with wrist actigraphy predicted impaired cognitive and behavioral performance.	Frequency of movement during sleep predicted impaired vigilance (Min > 5Mvts/night- R squared=.23, p=.00027) and (∑Movements Bed/ night- R squared=.19, p=.001) while consolidation of movements associated with impaired verbal (R squared=.16, p=.002) and memory skills (R squared=.21, p=.0035) and Obstructive Apnea Hypopnea Index (OAHI) was associated with more consolidation of movements (R squared=.38, p<.0001).
Knight & Dimitriou (2019)	Case control	ADHD: 17, Control:20	82%/18%	2 children with ADHD were on medication.	5–11 years	Raven's Coloured Progressive Matrices, British Ability Scale (BAS-III) from which the digits forward subtest was used to assess short-term verbal memory, Conner's Parent Report Scale (CPRS), Conner's Continuous Performance Test (CPT), CSHQ, Actigraphy. Limitations: Small sample size, smaller number of females, ADHD subtype, obtaining more nights' actigraphy data (weekend-weekday) from participants would strengthen measure, attentional task is limited in its application to real-world context.	To investigate the relationship among sleep, ADHD behaviors, and attention in school-age children with and without a diagnosis of ADHD.	Poor sleep quality affects developmental subgroups in different ways, for example for ADHD children, poor sleep worsens their predisposed attentional deficit (actigraphy measured time in bed and sleep latency showed trends of prediction for accuracy in CPT task R2=.46, p=.62), while for TD children it mimics ADHD behaviors (more sleep problems predicted a higher ADHD rating, R squared=.40, p=.05).
Hansen et al. (2013)	Case control	ADHD:38, ADHD+Anxiety disorder:25, Anxiety Disorder: 39, Controls: 35	63%/37%	Medication naive.	7–13 years	KSADS-PL, Children's Global Assessment Scale (CGAS), CBCL (Child Behavior Checklist) +TRF (Teacher Report Form), Wechsler Abbreviated Scale of Intelligence (WASI), CSHQ, Attention Network Test. Limitations: CSHQ not diagnostic tool for sleep disorders, no objective measure of sleep, diagnostic assessment based on parent reports only, no input from teachers collected, small sample size did not allow enough statistical power to identify relations between variables.	To examine associations between sleep problems and attentional and behavioral functioning in children with anxiety disorders, ADHD, combined anxiety disorder and ADHD and controls.	Sleep problems (increased CSHQ scores) were associated with reduced efficiency of the alerting attention system (warning signals had less effectin reducing reaction times during the test task) for all children (Beta coefficient of −1.84, p=.012) and with increased internalizing problems in children with anxiety disorders (p=.034).

(continued)

Table 5. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Gruber et al. (2011)	Case control	ADHD:11, Control: 32	63%/37%	4 children with ADHD on medication (askedto abstain for 48 hours before testing)	7–11 years	Petersen's puberty development scale, CBCL, Socio-economic Status questionnaire, Epworth Sleepiness Scale, Sleep Logs, Actigraph, Conner's Continuous performance test (CPT). Limitations: Small sample size, PSG only used post-CPT performance during 1 week, not able to be used as measure of sleep quality and duration, rapid withdrawal of medications beforebaseline could have affected results, brain circuits involved in the attention and arousal systemscould be focused on.	To assess impact of 1 hour of nightly sleep restriction over 6 nightson neurobehavioral functioning of children with ADHD and healthy controls.	Although the CPT scores of children in control group, deteriorated duringthe sleep restriction week, all scores nonetheless remained below the clinical cut off range of 60, however, for ADHD children, the significant deterioration of ~6-15 points inscores for Omission Errors, RT, change in RT, and Variability (@ $p = .05$ level) during the week of sleep restriction resulted in reduction in performance from subclinical levels of inattention to scores higher than or equal to a clinical cut off range of 60 on two-thirds of CPT outcome measures.
Bestmann et al. (2019)	Case control	ADHD:17, Control: 16 (children), 23 (adults)	100% males in all groups	12 children with ADHD were taking MPH but abstained for 48 hours prior to testing sessions.	9–12 years	Culture Fair Intelligence Test (CFT-20-R), battery for the assessmentof attention (KITAP), PSG. Limitations: Small sample size for both the patient and the control group.	To investigate associations between sigma power during sleep and cognitive performancein healthy and ADHD children.	Only healthy children displayed a positive correlation between sigma power and reaction times (highest $r = .733$, @ $p < .005$ over the F4 region) and a negative association between IQ and sigma power (highest $r = .511$ (not alpha corrected), @ $p < .05$ over the P3 region) indicatesa disturbed function of sleep in cognitive functions in ADHD.
Um et al. (2016)	Cross sectional	ADHD:28	78%/22%	Medication naïve.	6–12 years	Wechsler Intelligence Scale for Children-III (WISC-III), Matching Familiar Figure Test for Korean Children (MFFT-KC), Conner's Global Index-Parent version (CGI-P), PSG. Limitations: Lack of cognitive measures and PSG data for control group, sample sizes were small, majority subjects male, no subtyping of ADHD patients, first night effect of PSG not controlled.	To investigate the relationship between sleep parameters and cognitive function in drug-naïve children withADHD.	Slow wave sleep, stage 2 sleep, REM sleep, and limb movement index witharousals are predictors of cognitive function in ADHD patients. Slow Wave Sleep (Beta coefficient of .40, $p = .019$) and Limb Movement with Arousals (Beta coefficient of .37, $p = .032$) best predicted Verbal IQscores, whereas Conners GlobalIndex scores was predicted by percentage of REM sleep (Beta coefficient of –.55, $p = .002$).

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Table 5. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Zambrano-Sánchez et al. (2013)	Case control	ADHD:156, Control:111	67.4%/32.6%	Medication naive.	7–12 years	Paediatric Sleep Questionnaire (PSQ), Working Memory subscale from Wechsler intelligence scale for children (WISC-IV) toscreen Executive Dysfunction (ED). Limitations: Larger population needed to obtain stronger conclusions, long term prospective follow-up, no PSG done for confirming presence ofsleep disorders, covariates suchas psychological, socio- culturalfactors needed to reinforce results.	To determine the contribution of different types of sleep disordersin executive deficits among children with ADHD and typically functioning children.	A significant correlation was observed between PLMD frequency and ADHD-C type frequency ($r = .78$, $p = .05$) and between RLS frequency and ADHD-C and ADHD-H type frequency ($r = .65$, $r = .65$ respectively,$p = .05$), between ADHD-C children's with PLMD and coding values (WISC-IV) ($r = .75$, $p = .05$), between OSAHS and block design scores (WISC-IV) ($r = .64$, $p = .05$), and between ISH and digit values (WISC-IV) ($r = .57$,$p = .05$), for children with ADHD-I, significant correlations between ISHand each of coding ($r = .81$, $p = .05$), block designs ($r = .69$, $p = .05$), and digits scores ($r = .71$, $p = .05$).
Schmid and Wolke (2014)	Longitudinal	Infants:1120	50.6%/49.4%	Not mentioned.	Birth − 8.5 years	Neurodevelopmental Assessment, Tester's Rating of Child Behavior (TRCB), Kaufman's Assessment Battery for Children (K-ABC), Mannheimer Parent Interview (MPI), sleep was assessed throughparental report. Limitations: Datacollected in 1985–86. (standard of care has changed), sample consisted children referred to special neonatal care units after birth, results might not be generalizable to all infants requiring normal postnatal care, regulatory problems not assessedvia diaries, quality of parent–child interaction at school age not assessed or controlled for.	To investigate if persistent Regulatory Problems (RP) during the preschool are precursorsof ADHD and cognitive deficits in early childhood years.	RP at three measurement points (i.e., at 5, 20, and 56 months of age) werea predictor of lower IQ (K-ABC) at 8.5 years (small effect size: .17), poorer TEAM rating attention score (small effect size: .10), and of more activity (TRCB) (small effect size: .11), after controlling for confounding variables. RP at all three measurement points significantly increased the odds of inattention (MPI) (Odds Ratio (OR) 2.44), hyperactivity (MPI) (OR 3.09), and ofa DSM-IV diagnosis of ADHD (MPI) (OR 3.32).

(continued)

Table 5. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Saletin et al. (2017)	Case control	ADHD: 7, Control: 14	72%/28%	ADHD children withdrawn from psychostimulant medication for 2 weeks before and during the in-lab study.	10–12.9 years	Actigraph, PSG, Motor Sequence Task (MST). Limitations: Differences in sleep EEG reported might reflect not difference in ADHD but rather in learning-dependent changes in EEG, subjects recruited to be freeof disordered sleep thus study cannot address sleep disorders in ADHD's impact overnight improvements in motor learning, slow wave activity difference not assessed, participants withdrawn from psychostimulantsthroughout protocol, limiting ecological validity of their sleep.	To examine if the motor learning ability in ADHD children may be sensitiveto spindle-frequency EEG activity expressed during sleep.	The ADHD group expressed lower power in the slow (p=.023, d=−1.15)and fast (p = .049, d = −.98) spindle bands, with the greatest deficit observed for slow spindle activity. ADHD group had impaired MST precision in the evening as comparedto the TD group (Wald-χ^2=3.90, p = .048, d = 1.33), this effect was ameliorated in the morning following sleep (Wald-χ^2=.02, p=.88, d=.34) and MST precision was positively associated with slow spindle activityfor the ADHD group (χ^2=8.71, p=.003), but not for TDCs (χ^2=.50, p=.82).
Prehn-Kristensenet al. (2011)	Case control	ADHD: 16, Control: 16	100%/0%	12 children with ADHD took medication (MPH) however they discontinued its intake 48 hours prior to each testing session.	9–12 years	K-SADS-PL, CBCL, Culture Fair Intelligence Test Revised Vision (CFT-R), Diagnosticum für Cerebralschädigung (DCS), Pittsburgh Sleep Quality Index (PSQI), Procedural Memory Task, KITAP, PSG. Limitations: Limited sample size, no female participants, no social- emotionalfunctioning variable is measuredthat might effect learning.	To investigate sleep associated consolidationof procedural memory in ADHD children (sleepand wake conditions).	Children with ADHD showed improvement in motor skills after sleep compared to the wake condition [sleep condition: 202.4 ± 18.0; wake condition: 163.1 ± 14.3; t (15)=2.46, p=.026] and sleep-associated gain in reaction times was positively correlated with the amount of sleep stage 4 (r=.719,p=.002) and REM sleep-density (r=.589, p=.016) in ADHD.
Prehn-Kristensenet al. (2017)	Case control	ADHD: 16 (comorbid Oppositional Defiant Disorder), Control:16	100%/0%	11 children with ADHD took medication (MPH) however they discontinued its intake 48 hours prior to each testing session.	8–11 years	Sleep Self-report questionnaire, CSHQ, CBCL, Culture Fair Intelligence Test 20-Revised Version (CFT 20-R), Picture recognition task, eye-tracking andpupillometry, PSG. Limitations: Non-social stimuli could be used since faces can act as emotional stimuli, a balanced number of trials across immediately and delayed recognition measurement should be considered, inclusion of psychophysiological parameters during encoding are required.	To investigate the influence of sleep on thepicture recognition of emotional faces and theiraffective regulation in children with ADHD andcomorbid ODD (ADDH + ODD) in comparison to healthy children (sleep and wake conditions).	Pupillometry and behavioral data revealed that healthy children benefited from sleep compared towake with respect to face picture recognition (p < .001) ; in contrast recognition performance in patients with ADHD + ODD was not improved after sleep compared towake (p<.001).

(continued)

Table 5. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/outcomes
Weisner et al. (2017)	Case control	ADHD:17 (comorbid Conduct Disorder & Oppositional Defiant Disorder), Control:17	100%/0%	13 children with ADHD took MPH medication, but discontinued 48 hours prior to testing sessions.	8–12 years	Culture Fair Intelligence Test Revised Version (CFT-20-R), PSG, CSHQ, Sleep logs, KITAP (measuring attention), Sleep Self-report questionnaire, Pubertal Development Scale (PDS), Probabilistic Learning and Reversal task, Self-Assessment Manikin (SAM). Limitations: small sample, participants with comorbid social behavior disorder pose diagnostic entity separate from patients with only ADHD, results could be affected by circadian influences on learning performance, alertness, mood (valence, arousal).	To study if sleep fosters consolidation of behavior learned by probabilistic reward and whether ADHD patients with comorbid disorder of social behavior show deficits in this memory domain.	The drop in performance (in the probabilistic reward task) between sleep and wake in the ADHD children ($p = .264$, $d = .28$) did not differ but this difference was stronger during sleep than during wake in the control participants ($p = .042$, $d = -.51$), and this double difference was significant ($p = .028$, $d = .79$), which points that only the control participants showed sleep-dependent consolidation of rewarded behavior. For ADHD children there were only non-significant correlations of the performance drop with REM sleep ($r = .322$, $n = 17$, $p = .207$, $d = .68$) and non-REM sleep ($r = .138$, $n = 17$, $p = .597$, $d = .28$), in contrast, control participants showed a significant ($r = .441$, $n = 17$, $p = .076$, $d = .98$) correlation of performance drop with non-REM sleep (not with REM sleep), this points that retention of rewarded behavior over sleep did not correlate with sleep, especially not with REM sleep for the ADHD children, which was not the case for the control children.
Yürümez and Kılıç (2016)	Case control	ADHD:46, Control:31	100%/0%	Medication naïve.	7–13 years	CSHQ, Conner's Parent Rating Scale– Revised Long Form, Paediatric Quality of Life Inventory (PedsQL), Conner'sTeacher Rating Scale–Revised Long Form, WISC-R(Wechsler Intelligence Scale for Children-Revised), K-SADS-PL. Limitations: small sample size, lack of PSG data from all participants to rule out primary sleep disorders, parents' sleep habits and family stress not assessed, parents' ratings of sleep problems for children may be subject to rater bias and inaccuracy.	To assess the sleep behaviors, sleep problems and its frequency, and to evaluate the effect of sleep problems on quality of life for ADHD and control children.	PedsQL -Psychosocial subscale scores, completed by parents, are found significantly different for ADHD and control group (Mean 62, SD- 15.6 vs. Mean 79, SD- 10.6, $p < .001$) and between those children having sleep problems and those without sleep problems (Mean 62, SD- 15.6 vs. Mean 79, SD- 10.6, $p = .033$).

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Table 5. (continued)

Authors/ publication year	Study design	Participant characteristics				Primary measures, limitations and biases	Objective	Summary of main results
		Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age			Interventions/comparisons/outcomes
San Mauro Martín et al. (2018)	Case control	ADHD: 41, Control: 48	68.3%/31.7%	Not mentioned.	6–12 years	The Mediterranean Diet Quality Test for Children and Adolescents (KIDMED Index), Anthropometry, Physical Activity, Sedentary behaviors, Short Form Health Survey (SF-36), Sleep quality assessed by recording sleep duration (weekends/ weekdays). Limitations: Findings were not completely in line with previous literature in the topic and this could be due to the limited sample size.	To determine the association between environmental, nutritional, and body composition factors that may affect the pathogenesis and symptomatology of ADHD patients.	Low adherence to a Mediterranean diet might play a role in ADHD development. The average hours of sleep per week differed between ADHD and control group ($p = .031$),so did sedentary behaviors (time spent watching television and/or using computer/mobile/tablet ($p = .238$) and reading ($p < .001$)), same wasthe case for KidMed's final score ($p = .004$) and lastly for food items, observed in fish ($p = .001$), cereal ($p = .002$), no breakfast ($p = .007$), and commercially baked goods ($p = .01$) consumption.
Tong et al. (2016)	Cross sectional	Total children: 785 (ADHD symptoms 82)	52%/48%	Not mentioned.	9–13 years	Physical Activity Questionnaire for Older Children (PAQ-C), sleep environment, bedtime activities and screen time records, Child Eating Behavior Questionnaire (CEBQ), ADHD- RS-IV. Limitations: Study used questionnaire not interview-basedassessments to assess ADHD, physical activity measured by self-reported questionnaire rather than accelerometers, it is a cross sectional study, limiting ability to indicate causality.	To study the associations between ADHD symptoms in children and their associated lifestyle.	Children with ADHD symptoms showed more eating behaviors (□ = .04, $p < .01$), bedtime activities (□ = .05, $p < .05$) and more electronic devices in bedroom (□ = .01, $p < .01$) after controlling for children's gender, parents and children's age, parents' education level and annual household income.
Tong et al. (2018)	Cross sectional	Children: 934 (ADHD symptoms 82)	53%/47% (total participants), Within ADHD group: 14%/6%	Not mentioned.	9–12 years	ADHD Rating Scale-IV, Children's Sleep Habits Questionnaire, CBCL, Diet behaviors, Screen time. Limitations: Cross-sectionaldesign, limiting study's ability to draw causal inferences, sleep hours and sleep problemswere assessed by parent- reported rating scales rather than objective measures, study used a questionnaire and not an interview-based assessment to assess ADHD, data on medicationnot collected.	To determine the moderating effects of bedtime activities and depression/anxiety symptoms on the relationship between ADHD symptoms and sleep problems.	Bedtime activities and emotional problems had important moderating effects on the relationship between ADHD symptoms and sleep problems(for example interaction between screen time and ADHD predicted sleep duration on weekends (□ = −.111, $p < .05$), sleep onset delay(□ = −.058, $p < .05$) R squared = .094, and sleep-disordered breathing (□ = −.052, $p = .057$) R squared = .074and eating before bedtime played a moderating role in the relationship between ADHD and night waking (□ = .061, $p < .1$).

(continued)

Table 5. (continued)

Authors/ publication year	Study design	Participant characteristics				Primary measures, limitations and biases	Objective	Summary of main results
		Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age			Interventions/comparisons/outcomes
Peralta (2018)	Longitudinal	Children: 817	51%/49%	Not mentioned.	4–7 years	Conners' Parent Rating Scales and the Strengths and Difficulties Questionnaire, parental report of time spent watching TV, sleeping and engaging in cognitivestimulating activities. Limitations:Use of parental questionnaires to assess variables and thereby misclassification subject to inaccuracy, children who had longer breastfeeding, higher maternal IQ, and higher parentaleducation levels than those who did not participate, no information on pharmacologicalor nonpharmacological.	To analyse associations between time spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity (assessed at 4 years) and ADHD symptoms and behavior problems, both assessedat 7 years, in ADHD-free children at baseline.	A shorter sleep duration and less time spent in cognitively stimulatingactivities were associated with an increased risk of developing ADHDsymptoms (p = .006), in addition, engaging in less cognitively stimulating activities at 4 years was associated with an increased risk of developing ADHD symptoms ($p < .001$) and developing behavioral problems (p = .005).
Jackson and Vaughn (2017)	Longitudinal	Children: 3800	52%/48%	Not mentioned.	1–10 years	Parental reports for sleep duration, sleep problems, preteen delinquency, Conner's Teacher's Rating Scale-Revised Short Form, CBCL. Limitations: Limited items pertaining to sleep quality,measures (with the exception of teacher plus parent report of ADHD), were based on parental/ caregiver report, continuation of delinquency beyond preteen years could not be definitively determined due to data limitations, lack of experimentaldesign, high-risk families overrepresented in sample.	To examine associations between sleep patterns, ADHD, and delinquency.	There is a significant association associations between ADHD symptomatology, ADHD diagnosis, and preteen delinquency, with oddsratios ranging from 2.38 to 8.10 (p < .001), additionally accountingfor both ADHD symptomatology and ADHD diagnosis, the negative association between sleep duration and preteen delinquency is significant(OR = .85, p = .011).

Sleep-Related Interventions and their Impact on Sleep and Daytime Function in ADHD

Details of the studies reviewed on sleep interventions and their impacts on daytime function in ADHD are detailed in Table 2.6. When the behavioral and neurocognitive effects of neurofeedback were compared to stimulant medication and physical activity in 7 to 13-year-old children with ADHD (n = 92) at 6 months' follow-up parents and teacher reported improvements for neurofeedback on sleep quality (assessed through the Sleep Disturbance Scale; Geladé et al., 2018). A study assessing the effectiveness of cognitive rehabilitation of response inhibition in improving the quality of sleep and behavioral symptom of children with ADHD (7–12 years) revealed significantly lower scores on the Pittsburgh sleep quality index (PSQI) and on the three features of hyperactivity, impulsivity and attention deficit (measured through parent rated Conner's questionnaire) for the treatment group (n = 10) compared to the control group (n = 10) (Yazdanbakhsh et al., 2018). With regard to techniques based on sensory integration, Hvolby and Bilenberg (2011) studied the effect of using a Ball Blanket aimed at stimulating both the sensation of touch and the sense of muscle and joint (and thereby leading to sensory impressions that transmit inhibitory impulses to the central nervous system) on sleep of children with ADHD (n = 21, 8–13 years). The findings revealed that the use of Ball Blankets for 14 days improves sleep onset latency, individual day-to-day variation and number of awakenings to a level comparable with those found in the healthy control children (n = 21) and reduces the frequency of nights in which the child spends more than 30 minutes falling asleep from 19% to 0%.

The impact of a behavioral sleep intervention in children with ADHD (n = 244, 5–12 years) in a randomized controlled trial revealed significant parent-rated decrease in moderate/ severe sleep problems at 3 months' post treatment; daily sleep duration measured by actigraphy was also increased in the intervention group children, and approximately a half to one-third of

the beneficial effects of the intervention on ADHD symptoms was mediated through improved sleep at 3 and 6 months follow-up (Hiscock et al., 2015). A brief behavioral sleep intervention, comprising of two clinical consultations and a follow-up phone call covering sleep hygiene and standardized behavioral strategies, in 5 to 13 years old children with ADHD with comorbid Autism Spectrum Disorder, led to large improvements in parent- rated sleep problems at 3 and 6 months for the treatment (n-28) group compared with the usual care (n = 33) group (Papadopoulos et al., 2019). Further, the intervention group (n = 28) also had small to moderate improvements in parent- rated psychosocial quality of life, ADHD symptom severity and child behavior (Papadopoulos et al., 2019). When 20 children (8–12 years) in each group for ADHD, Anxiety and ADHD + Anxiety were treated with cognitive behavioral therapy for anxiety, this lead to significant decrease in anxiety along with improvement in sleep latency and marginal decrease in total amount of sleep problems for the treatment groups (Beriault et al., 2018).

Keshavarzi et al. (2014) showed that a 12-week sleep training program followed by parents of children with ADHD (8–13 years) led to significant improvements over time for the intervention group (n = 28) in sleep problem areas such as being afraid of sleeping in the dark, sleeping alone, sleeping too little, sleeping the right and the same amount, bed wetting and sleeping restlessness, along with decrease in the duration of awakenings after sleep onset and increases in total sleep time. Parents of children in the intervention group also reported improved in physical and psychological well-being, moods and emotions, parent relations and home life, school environment, and social acceptance for their children. Peppers et al. (2016) investigated the effect of a 20-week intervention involving following a patient specific sleep hygiene routine to promote sleep and reduce ADHD symptoms among children (5–11 years): participants receiving sleep hygiene interventions (n = 23) had significant reduction in ADHD symptoms and a significant improvement in sleep quality (Peppers et al., 2016). Corkum et al. (2016) investigated the effect of a distance intervention for insomnia in children (aged 5–12

years) with ADHD, which included parents being mailed intervention manual, diaries for tracking sleep and intervention implementation, and a reward chart with stickers and 5 weekly telephone sessions for coaching in the sleep intervention steps. Results from this study indicated significant improvement in three areas of sleep onset latency, bedtime resistance and sleep duration in the treatment group (n = 30) as assessed through parent rating and in the area of sleep onset latency (Corkum et al., 2016).

The effect of a 5-week elimination diet on physical and sleep complaints in children with ADHD (treatment group n = 15) were investigated by Pelsser et al. (2010) who reported a 77% decrease in the number of physical and sleep complaints. In another study, the effect of tryptophan enriched cereal intake on sleep of children with ADHD (n = 6), Cerebral Palsy (n = 9) and Autism Spectrum disorder (n = 7) was studied; actual sleep time, sleep efficiency and immobile time improved in children with ADHD as measured through wrist actigraphy (Galán et al., 2017). The effect of 10 weeks' treatment with a polyunsaturated acid mixture on children with ADHD's behavior (n = 78, 40 in treatment group) showed significant improvement in quality of life, ability to concentrate, hemoglobin levels and sleep quality (Yehuda et al., 2011). Sonne et al. (2016), studied the effect of MOBERO, a smartphone-based system that assists families in establishing healthy morning and bedtime routines in a 2-week intervention with children with ADHD (n = 13, 6–12 years). The intervention was associated with 8.3% improvement in sleep habits, including positive change in seven of the eight CSHQ subscales (bedtime resistance, sleep duration, sleep anxiety, night wakenings, parasomnias, sleep disordered breathing and daytime sleepiness) and 16.5% reduction in core ADHD symptoms (Sonne et al., 2016).

Table 2.6 *Summary of Thirteen Included Studies Focusing on Non-Pharmacological Interventions and Their Impact on Sleep and Overall Functioning in Children with ADHD.*

		Participant characteristics						Summary of main results
Authors/ publication year	Study design	Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Interventions/comparisons/ outcomes
Geladé et al. (2018)	Randomized control trial	ADHD:92	76%/24%	36 children with ADHD were allocatedto medication intervention (MPH), however at 6-month follow-up, 21 were still using medication and 6 had discontinued.	7–13years	Auditory oddball, stop-signal, and visual spatial working memory tasks, Strength and Difficulty Questionnaire (SDQ) and Strengths and Weaknesses of ADHD symptoms and Normal Behavior Scale (SWAN), Sleep Disturbance Scale for children (SDSC). Limitations: Naturalistic controlled follow up, so potentially unknown factors might have improved outcomes, small sample limiting statistical power, statistical power of sensitivity analyses was reduced due to smaller sample size.	To compare behavioral and neurocognitive outcomesat a 6-month naturalistic follow-up of a randomized controlled trial for neurofeedback (NFB), methylphenidate (MPH), and physical activity (PA).	Improved inhibition in MPH compared to NFB ($p<.001$ after intervention and $p=.040$ at follow-up) and faster response speed in NFB compared to PA during the stop-signal task ($p=.012$). Results demonstrated comparable improvements in sleep quality for all interventions.
Yazdanbakhsh et al. (2018)	Quasi-experimental intervention study	ADHD: 20 (10 in treatment group, 10in control group)	60%/40%	Currently not medicated.	7–12years	Conner's Parents and Teacher's Rating Scale (CPRS), Pittsburgh Sleep Quality Index (PSQI). Limitations: Limited sample size, absence of control group with another treatment form and also follow up outcomes for interventions.	To measure the effectiveness of 12 sessions of cognitive rehabilitation of response inhibition in improving the quality of sleep and behavioral symptom of children with ADHD.	Intervention bettered the quality of sleep (effect size: .63, $p < .001$) and behavioral symptoms in ADHD (effect size: .58, $p<.001$).
Hvolby and Bilenberg (2011)	Case-control intervention study	ADHD: 21 control: 21	90%/10%	Children with ADHD were on medication (Stimulant, Atomoxetine, Dexamphetamine, Stmulant + Atomoxetine, Melatonin, Alternative medicine).	8–13years	Actigraphy recordings, parent completed sleep diary. Limitations: Relatively small sample size, short lenghth of time for use of blanket, subtypesof ADHD not identified in sample, effect of medication not examined.	To assess the effect of using a ball blanket for 14 nights and 14 nights without it (pre & post), through actigraphy recordings and parental reports.	Results indicated improvements among ADHD children in sleep onset latency (the average sleep onset latency was 23.1 minutes, which fell to 14.0 minutes when using the Ball Blanket—a fall of 39.4%, $p<.002$), the proportion of single nights when more than 30 minutes were spent falling asleep fell from 27.7% to 14.8% when using the blanket($p<.003$), which is the same level as the healthy control children, parents reported that with the use of the ball blanket sleep onset latency fell from an average of 36.7 to 26.9 minutes, which is an improvement of 26.7%($p<.001$).

(continued)

Table 6. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Hiscock et al. (2015)	Randomized controlled trial	ADHD: 244	84%/16%	211 children were on medication (MPH, Atomoxetine and Clonidine).	5–12 years	ADHD rating scale, CSHQ, Actigraphy, Strengths and Difficulties questionnaire, Paediatric quality of life inventory 4.0), Daily Parent Rating of Evening and Morning Behavior (DPREMB),working memory test battery, parent mental health (depression anxiety stress scales). Limitations: Parents not blinded about randomization results, leading to possible overestimation of improvements, response rate at 3 months was low.	To study the effect of a sleep hygiene Intervention and standardized behavioral strategies in 2 fortnightly sessions and a follow up phone call on the ADHD child's sleep problems, ADHD symptoms, functionality and working memory.	A brief behavioral sleep intervention modestly improved the severity of ADHD symptoms ((at 3 and 6 months follow-up) $p = .03$, effect size −.3, and $p = .004$, effect size −.4, respectively), compared to children in the control group, intervention children had fewer moderate-severe sleep problems at 3 months (56% vs. 30%; adjusted odds ratio .30, $p < .001$) and 6 months (46% vs. 34%; adjusted odds ratio- .58; $p = .07$), Working memory was found to be higher in the intervention children compared with control children at 6 months. And daily sleep duration was higher in the intervention children at 3 months (effect size .2) and 6 months (effect size .3).
Papadopoulos et al. (2019)	Randomized control trial	ADHD comorbid ASD: 61 (28 in treatment group and 33 in control group)	85%/15% (Intervention) 90%/ 10 % (usual care)	53 children with ADHD were on medication (MPH (long and short acting), Atomoxetine and Clonidine).	5–13 years	CSHQ, Strength and Difficulties questionnaire, ADHD rating scale- IV, Paediatric Quality of Life questionnaire, Depression Anxiety Stress scale (for parents). Limitations: Reliance on parent's reports for ASD assessment, rather than objective assessment tool, sample had average intellectual ability, so children with clinical level deficit not explored, parents not blinded for interventions possibly affected ratings, small sample size.	To study the efficacy of a brief behavioral sleep intervention.	Results showed improvements in sleep problems (CSHQ total score, 3 months (effect size- .7) other sub scales also showed improvements such as sleep onset delay, effect size- .9 at 3 months post intervention; sleep duration, effect size- .8 at 6 months post intervention and parasomnias, effect sizes- .6 and .7 at 3 and 6 months post intervention).

(continued)

Table 6. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Bériault et al. (2018)	Exploratory Intervention study	ADHD:20, ADHD+Anxiety:20, Anxiety: 20, Control: 9	73%/27%	17 children with ADHD were on medication, 18 children with ADHD+ Anxiety were on medication (Psychostimulants, Atomoxetine and Risperdone).	8–12years	CSHQ, Anxiety Disorders Interview Schedule for children, ADHD rating scales- IV, Multidimensional Anxiety Scale for children (MASC). Limitations: Limited sample size, groups not compared on socio-economic variables, sleep was assessed by parent questionnaires, rather than objective measures.	To examine the effectof cognitive-behavioral therapy (CBT) for anxietyon sleep problems in ADHD children with comorbid anxiety disorders and to examinethe sleep problems in children with ADHD and ADHD+Anxiety.	Total score and number of problems in the CSHQ had significantly higher values in each clinical group compared with the control group ($p<.001$ & $p<.05$ respectively), anxiety related to sleep were significantly greater in the three clinical groups compared with the controls($p<.01$) and CBT led to significant outcomes for daytime somnolence (effect size: .36), Total score in CSHQ (effect size: .36) reduction in the first order severity score in the Anxiety Disorders Interview Schedule (effect size: .93), Total score forMASC (effect size: .60).
Keshavarzi et al. (2014)	Randomized control trial	ADHD: 40 (20 in control and 20 intrial)	95%/5%	All children with ADHD were on medication (MPH).	8–13years	CSHQ, KID-Screen, parent view and children view, Strength and difficulties questionnaire. Limitations: Limited sample size,no cognitive or ADHD-related assessments, no objective sleep assessment, parents not blindedfor intervention group.	To study the effect of 12 week randomized control trial for sleep training on emotional,social and behavioral functioning in childrenwithADHD.	Intervention group improved sleep quantitatively and qualitatively ($p<05$), intervention receiving children reported improvements in mood, emotions, and relationships ($p<.05$). Parents reported that their children improved in physical and psychological wellbeing, mood, emotions, relationships, and social acceptance ($p<.05$).
Peppers et al. (2016)	Intervention study	ADHD: 53 (23: treatment group)	57%/43%	All children with ADHD were on medication (MPH, Amphetamine and non-stimulant).	5–11years	CSHQ, Vanderbilt ADHD parent scale. Limitations: Small samplefor intervention from the full number of participants.	To study the effect of a 20-week pilot project usinga sleep hygiene routine to assess sleep and ADHD symptoms.	The CHSQ and Vanderbilt scores indicated a significant improvement in sleep quality and reduction in ADHD symptoms after implementation of the sleep hygiene routine (CHSQ: $p<.001$, d=.928; Vanderbilt Questions 1–9: $p<.001$, d=.473; Vanderbilt Questions 10–18: $p=.004$; d=.329).
Corkum et al. (2016)	Randomized control trial	ADHD: 61 (30 in treatment group and 31 in waitlist control group)	46%/54%	14 children with ADHD were on medication.	5–12years	Actigraphy, CSHQ, CBCL, Sleep Evaluation Questionnaire,K-SADS-PL. Limitations: Parents were not blind to the intervention conditions which may have affected their ratings, adherence to actigraphy was low,limiting power of analysis, small sample size.	To study the effect of five-session manual and weekly telephone coach support on the children's sleep and psychosocial functioning.	Results indicated improved sleep onset (effect size: .23, $p=.017$) improved parent rated CBCL internalizing (effect size: .30, $p<.001$) and externalizing scores (effect size: .27, $p<.001$).

(continued)

Table 6. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Pelsser et al. (2010)	Randomized control trial	ADHD: 27 (15 in treatment group and 12 in control group)	76%/34% (Intervention group), 81%/19%	Medication naive.	3.8–8.5 years	Pre-post assessment via Physical Complaints Questionnaire (includes 2 sleep questions). Limitations: Older children would better describe physical symptoms, sleep related movements disorders not explored in the sample, ADHD subtype not explored.	To investigate the effects of a 5 week elimination diet on physical and sleep complaints in children with ADHD.	The number of physical (headaches or bellyaches, unusual thirst or unusual perspiration) and sleep complaints was significantly decreased in the diet group compared to the control group ($p < .001$), with a reduction inthe diet group of 77% ($p < .001$, effect size = 2.0) and in the control group of 17% ($p = .08$, effect size = .2).
Galán et al. (2017)	Intervention study	ADHD: 6, ASD: 7, Cerebral Palsy: 9	50%/50% (ADHD group), 42%/58% (ASD group), 55%/45% (Cerebral Palsy group)	Children with ASD: Risperidone, Aripiprazole and Paliperidone, Cerebral palsy took low doses of Benzodiazepine, Tryhexyphenidyl, Polyethylene or Antihistamines and patients with ADHD took Methylphenidate, long-acting Methylphenidate or Fluoxetine.	ADHD group: mean-8.67(SD-2.73) years	Actigraphy records. Limitations: Small sample size, not a randomized controlled trial.	To study the effect of Tryptophan enriched antioxidant cereals on sleep problems among children with ADHD, ASDand Cerebral Palsy.	Assumed sleep was significantly higher when the target diet was taken for dinner rather than only breakfast, or control, or basal week ($p < .05$), sleeplatency levels were significantly($p < .05$) lower than control levels when children took target diet for dinner, Sleep efficiency levels were significantly ($p < .05$) higher in diet taken in Dinner-week than in basal, control and diet taken in breakfast-week and immobile time improved ($p < .05$) in children with ADHD ingested tryptophan-enriched cereals at dinner than in control week.
Yehuda et al. (2011)	Intervention study	ADHD: 78(40 in treatment group and 38 in placebo group) Control: 22	100%/0%	Not	9–12 years	Questionnaire completed and hemoglobin level tested pre-post treatment. Limitations: No questionnaire or tool to assessother psychological variable.	To the study the effect of a 10 week polyunsaturated acid mixture on cooperation, mood, concentration, homework preparation, fatigue and sleep quality among ADHD children.	Results indicated significant improvement in quality of life, ability to concentrate, sleep quality and hemoglobin levels($p < .05$ & $p < .01$ level of significance).
Sonne et al. (2016)	Intervention study	ADHD: 13	70%/30%	7 children with ADHD were on medication	6–12 years	The Daily Assessment Application (DAA), ADHD Rating Scale-IV, CSHQ. Limitations: Small sample.	2-week intervention with smartphone based application for bedtime routines/2 week baseline phase.	Use of MOBERO was associated with a 16.5% reduction in core ADHD symptoms $p < .05$, Cohen's d = .73 and an 8.3% improvement in the child's sleep habits ($p < .05$, Cohen's d = .67).

ADHD Pharmacotherapy Effects on Sleep

Studies reviewed for the impact of ADHD medication on sleep are detailed in Table 2.7. A focus group study with parents (n = 16) of children with ADHD (3–12 years) found that parents commence and continue pharmacotherapy for their children due to improvements in academic performance and social interactions, and cease therapy after their children experienced side effects including appetite suppression, weight-loss and sleep disturbances (Ahmed et al., 2017). Bock et al. (2016) stated that clinicians (n = 67) reported that 39% of patients with childhood ADHD seek over the counter or prescription medication for their sleep problems. Further sleep medication use (melatonin 14% and clonidine 9%) in 5 to 13-year-old children with ADHD (n = 257) was associated with their intake of ADHD medication, combined ADHD subtype and internalizing/externalizing comorbidities (Efron et al., 2014).

In children with ADHD (n = 163, 7–11 years), increased Methylphenidate (MPH) dose is associated with increased sleep problems, particularly for lower weight/BMI; 23% of children without pre-existing sleep problems were reported to have sleep problems at the highest MPH dose (Becker, Froehlich, et al., 2016). Childress et al. (2009) reported that psychiatric side effects, events including insomnia occurred more often in patients assigned to the higher doses of Dex-MPH Immediate release (20, 30 mg/day) in a study including 253 children with ADHD between 6 and 12 years of age. For similar age group participants, Lee et al. (2012) reported MPH had a negative effect on later bedtimes, wake-up times and total sleep times for children with ADHD (TST was reduced by about 17 minutes on weekdays and 29 minutes at weekends, no difference between higher or lower doses, total n = 93). Further, parent-reported side effect ratings (n = 157) revealed significantly more insomnia in the MPH treatment group as compared to the placebo group (Lee et al., 2011). Further in another similar age group of children with ADHD on MPH (n = 12) were reported to be significantly sleepier

as the morning progressed, although at no point did they feel sleepier than 11 medication naive children (Cockcroft et al., 2009). When outcomes for MPH and Vitamin D supplement were assessed in children with ADHD (n = 25, 5–12 years), improvements in parent ratings for evening behaviors including getting ready for bed and falling asleep were reported compared to a control group (n = 29) receiving MPH and placebo (Mohammadpour et al., 2018). Omega-3 supplementation with MPH for children with ADHD (n = 33, 6–12 years) revealed no significant sleep related drug complication differences when compared to MPH and placebo group (n = 33; 2.9 &4 % respectively) (Mohammadzadeh et al., 2019). In a Venlafaxine versus MPH effect study, side effects of insomnia were more frequently observed in the MPH treatment group (n = 8, 6–12 years) (Zarinara et al., 2010). Sonuga-Barke et al. (2009) showed that while sleep problems significantly increased as a function of MPH treatment among children with ADHD, children who showed sleep-related adverse events also showed appetite-related adverse-events as reported by parents (total n = 184, 6–12 years).

Regarding MPH formulation, a handful of studies have examined the impact on sleep parameters. For extended release MPH, a trial with children with ADHD (n = 24, 6–12 years) comparing polysomnography and CSHQ results before and after the treatment found that sleep onset latency did not change, but that the number of awakenings decreased, and the percentage of stage 2 sleep increased during treatment (Kim, 2010). Switching from MPH- Immediate release to MPH extended release revealed no changes in sleep in 102 six to twelve-year-old children with ADHD (Kim et al., 2011). An efficacy and tolerability assessment of MPH transdermal formulation versus MPH immediate release found that both medications were well tolerated with only mild reductions in sleep onset latency (Pelham et al., 2011). A placebo controlled 3-week trial for assessing MPH extended release (ER) and delayed release (HLD200) revealed insomnia (>10%) as a commonly reported treatment emergent adverse

effect for both the 6 to 12 years aged treatment groups (n = 81) as compared to placebo (n = 80) (Pliszka et al., 2017).

Findings of adverse effects of MPH on sleep are not universal. Faraone et al. (2009) reported that neither once-daily oral (n = 89) nor transdermal formulations (n = 98) of methylphenidate reliably elicit sleep problems or influence the severity of such problems when they occur along with no significant effect of dose in 6 to 12 year olds with ADHD. On similar lines in the same age group, Ashkenasi (2011) reported that transdermal MPH patch wear times (9, 10, 11, and 12 hours per day) exerted no significant effect on sleep latency or total sleep time on children with ADHD (n = 26). A study investigating long-term tolerability of transdermal MPH found no apparent overall effect on sleep behavior for the children (n = 327, 6–12 years) as per parent reports on CSHQ (Findling et al., 2009). Chin et al. (2018) showed significantly increased total sleep time and reduced periodic limb movement index along with parent-reported reduction in bruxism and snoring in ADHD-Inattentive children (n = 35), as well as nightmares in ADHD-Combined presentation (n = 36) as an effect of MPH. Morash-Conway et al. (2017) report that following MPH treatment, sleep duration in children with ADHD (n = 21) was positively related to performance improvement on an executive attention task. Ricketts et al. (2018) found no deleterious effect of MPH on sleep (n = 143) and that combined treatment with stimulant medication plus behavior therapy (n = 144) was associated with statistically significant reductions in sleep problems.

A number of studies have examined the effects of MPH on circadian function in children with ADHD. Ironside et al. (2010) reported that for children with ADHD on MPH, mean motor activity levels (Mesor) were elevated during the down interval time (the sleep-onset latency period after lights out when children were in bed trying to sleep; n = 16, 6–12 years). A prospective 24-week observational study to assess trends in morning salivary cortisol

levels among children with ADHD on MPH revealed that for these 6 to 12-year-old children (n = 50) morning salivary cortisol level increased significantly during the first month of MPH treatment, before the level subsequently dropped to an intermediate level that was not significantly different from either the baseline or 1-month level over the 6-month course of treatment (Wang et al., 2017). Slama et al. (2015) found a positive effect of MPH in CPT assessment for children with ADHD (total n = 36, 7–12 years), with faster and less variable reaction times than under placebo during late afternoon, 8 hours after medication. Medication with MPH has also been reported to shift heart rate variability markers toward levels of normal controls (Buchhorn et al., 2013).

Three included studies examined the impacts of amphetamines on sleep measures in children with ADHD. Giblin and Strobel (2011) studied the effects of Lis dexamphetamine (LDX) on sleep in children with ADHD (treatment n = 16, 6–12 years) using polysomnography, actigraphy and subjective sleep measures and reported that LDX did not contribute to sleep disturbances as measured by both objective and subjective sleep parameters. However, 27% of children with ADHD treated with LDX (n = 129, 6–12 years) experienced the treatment emergent side effect of insomnia (Wigal et al., 2009). On similar lines for the same age group, Wigal et al. (2012) found one of the significant side effects of "trouble sleeping" for LDX, although stimulant-naïve children (n = 13) had significantly greater difficulty sleeping compared to those previously exposed to stimulants (n = 14). Examining the effects of non-stimulant ADHD medication on sleep parameters, Guanfacine treatment among 6 to 12 years' children, polysomnographic evaluation found that morning administration of Guanfacine extended release medication (n = 11) had an untoward effect on the polysomnographic sleep outcome measure of total sleep time and total time in slow wave sleep (found to be shorter) compared with morning administration of placebo (n = 16) (Rugino, 2018). For the same age group ADHD children, Guanfacine extended release use was not associated with

subjective self-report of daytime sleepiness for morning (n = 107) or the evening (n = 114) administration groups (Young et al., 2014), although the same study reported somnolence as one of the frequent treatment emergent adverse effect. Somnolence was also reported as one of the primary adverse events associated with Guanfacine extended release treatment (n = 138, 6–12 years) of children with ADHD by Connor et al. (2010). For treatment with atomoxetine, Montoya et al. (2009) demonstrated significantly more frequent adverse event of somnolence (24%) for atomoxetine compared to placebo (total n = 113). However, a subjective ADHD-related morning and evening behavior rating scale (including an independent item: difficulty falling asleep) for 6- to 12-year-olds children yielded improved scores for the treatment group (n = 54) using Atomoxetine as compared to 51 receiving placebo (Wehmeier et al., 2011).

For other pharmacological treatments, one randomized controlled trial (RCT) reported that L-DOPA improved restless leg syndrome and periodic leg movement syndrome although it did not improve ADHD symptoms, sleep parameters, or neuro-psychometric measures in 7- to 12-year-old ADHD patients (n = 15) when compared to 14 receiving placebo (England et al., 2011). However, within a similar age group, Ferri et al. (2013) found that Levodopa did not modify leg movement time structures for children with ADHD yet improved sleep latency (treatment n = 10). Hoebert et al. (2009) reported melatonin treatment to be effective in 88% of cases of children with ADHD and chronic sleep onset insomnia (n = 105, 6–12 years). Melatonin treatment in ADHD patients (children under 12 years n = 42, 6–12 years) also treated with MPH and who developed sleep problems was found to be effective in improving sleep problems in 60.8% of the patients, with this efficacy was similar in males and females and in children when compared to adolescents (Masi et al., 2019). An 8-week, placebo-controlled study to investigate the efficacy of zolpidem for the treatment of insomnia associated with ADHD revealed no significant change in sleep latency between base- line and week 4, and no significant difference in scores for the CGI (Clinical Global Impression) scale were observed

between weeks 4 and 8 among the age group of 6 to 11year children (treatment n = 136) (Blumer et al., 2009). In an objective sleep quality study, actigraphy data indicated that ADHD boys (8– 12 years) who consumed L-theanine (n = 46) obtained significantly higher sleep percentage and sleep efficiency scores, along with a non-significant trend for less activity during sleep (defined as less time awake after sleep onset) compared to 47 of those in the placebo group (Lyon et al., 2011). Finally, Blader et al. (2009) reported that children with ADHD (6– 13 years) whose disruptive psychosocial behaviors were under- responsive to stimulants and were treated with divalproex (n = 15) tended to have higher rates of trouble falling asleep than children treated with placebo (n = 15).

Table 2.7 *Summary of Forty-Two Included Studies* Focusing on Pharmacotherapy and its Effect on Sleep in Children with ADHD.

		Participant characteristics						Summary of main results
Authors/ publication year	Study design	Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Interventions/comparisons/ outcomes
Ahmed et al. (2017)	Qualitative analysis of focus group discussions.	16 parents of ADHD children	For parents: 56%/44%	All children with ADHD whose parents participated were on prescription medication (methylphenidate, dexamphetamine, or atomoxetine).	3-12 years (parent age: 32–55)	Focus group (3). Limitations: Study not designed to address specific hypothesis, but a qualitative investigation, small number of participants, from a specific geographic urban location.	NA	Parents elected to cease pharmacotherapy after reportedside effects including appetite suppression, weight loss, and sleep disturbances.
Bock et al. (2016)	Survey	67 respondent pediatricians (39% reported prescribing medication for ADHD)	N/A	N/A	NA	26-item survey. Limitations: Cross-sectional 6-month recall design subject to recall bias, bias to report socially desirableinformation, small sample.	NA	89% and 66% of the clinician respondents frequently use pharmacotherapy to treat paediatric sleep problems; few (20%) have received any trainingin this area. Melatonin (73%), OTC antihistamines (41%), antidepressants (37%), and benzodiazepines (29%) were themost commonly recommended medications.
Efron et al. (2014)	Cross sectional	ADHD:257 (57 on sleep medication)	86%/14%	53 children with ADHD were on medication	5–13 years	CSHQ, ADHD Rating Scale IV), ADHD medication use, Anxiety Disorders Interview Schedule for Children/Parent version IV, parent mental health (Depression Anxiety Stress Scale), Sleep log. Limitations: Study unableto ascertain indication for medication prescription, no control group, sample had children recruited for sleep-related studies, with 62% having moderate/severe sleep problems by parent report.	This study aimed to describe sleep medication use, as well as associated child and family characteristics in school-aged children with ADHD.	Children using ADHD medication were three times ($p = .05$) more likely to use sleep medication than children not taking ADHD medication; while children with combined-type ADHD were 2.5 times ($p = .04$) more likely than children with inattentive-type ADHD to use sleep medication and children with co-occurring internalizing and externalizing concerns were two times ($p = .04$) more likely to use sleep medication.
Becker, Pfiffner,et al. (2016)	Randomized Controlled trial	ADHD-In: 120, ADHD-Com.: 43	72%/28%	Stimulant naïve.	7–11 years	DISC-IV-Parent version, Vanderbilt ADHD parental version, Pittsburgh side effects rating scale. Limitations: Medication could not start from highest dose, or from placebo to highest dose, single parent-report item sleep measure used, results limited to initial medication titration, no examination of sleepduring MPH maintenance or long-term; structure surrounding bedtime, parenting behaviors, or metabolism of MPH not explored, more ADHD-I children.	4-week, randomized, double-blind, placebo-controlled trial of once-daily (long-acting) methylphenidate (MPH)'s effect on predictors of sleep problems and other side effects.	Rates of reported sleep problems during the titration were 8.0% on placebo (7.4% moderate, 0.6%severe), 17.8% on low MPH dose(14.7% moderate, 3.1% severe), 14.7% on medium MPH dose (10.4% moderate, 4.3% severe), and 24.6% on high MPH dose (16.0% moderate, 8.6% severe). Weight (BMI) was significantly negatively associated with sleep problem scores on the low dose(Effect size = .03), medium dose (Effect size = .03), and high dose (Effect size = .04).

(continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Childress et al. (2009)	Randomized controlled trial	ADHD: 253	64.4%/35.6%	Medication naïve (175) or not treated with MPH-related medication in last 1 month (74).	6–12 years	Recording of AEs, serious adverse events, vital signs, body weight, electrocardiogram (ECG), physical examination, hematologyparameters, blood chemistry, andurinalysis, Conner's ADHD ratingscales-parents and teachers (CADS-P&P), Global ImpressionsScale (CGI-S). Limitations: In this forced-dose titration study, some subjects may not have beentreated with optimal dose of d-MPH XR, the short, 5-week, duration does not allow for extrapolation of findings to long-term ADHD outcomes.	To examine the efficacy of 5 weeks, three doses of (10, 20, or 30 mg, once daily) dexmethylphenidate hydrochloride (HCl) extended-release (d-MPH XR; Focalin-XR)	All three doses of d-MPH XR were significantly more effective than placebo in improving ADHD symptoms as confirmed by parent ($p < .001$ for all three d-MPH XR groups). Decreased appetite and insomnia were themost frequently reported AEs leading to discontinuation (1.1%in "all d-MPH XR" group).
Lee et al. (2011)	Randomized controlled trial	ADHD: 157	All respondents were mothers	Previously prescribed MPH.	6–12 years	Conner's Global Index for parents (CGI-Parents) and teachers (CGI-Teachers), Barkley Side Effects Rating Scale (SERS). Limitations: 0.5 mg/kg MPH for a 1-week period deviates fromcommon clinical practice, use of only parent report for side- effects data. parents' treatment expectations/presence of parental ADHD not evaluated, majority of evaluations by mothers or both parents together, no data on teachers' gender preventing using gender as a covariate.	Random assignment, either placebo or 0.5 mg/kg/day MPH's efficacy for 1 week and the correlationsof the side effects.	The greater "mood/anxiety" side effects on methylphenidate and placebo, the less the parents observe improvement of their children while treated with methylphenidate. Significant negative correlations were observed between the CGI-P response to MPH and the SERS parent ratings (placebo - MPH) for *irritability, prone to crying*, and *anxiousness* ($p < .005$). The poorer the therapeutic response, the higher these side effects were.
Lee et al. (2012)	Randomized controlled trial	ADHD:93	63 were eligible out of which (88%/12%)	Participants were not on medication 4 weeks prior to the study	6–12 years	Clinical Global Impression of Severity (CGI-S) and the Clinical Global Impression-Improvement scale (CGI-I), Adverse events (AEs) chart, Sleep diary. Limitations: Study used sleep diary rather than objective measures, study used flexible titration method and did not divide the subjects into parallel-groups as per dose of MPH/age,lack of blinding, more than 30%of subjects did not complete procedure.	To study the effect of MPH (extended release and immediate release preparations) on sleep parameters.	MPH had negative impacts on sleep among young ADHD children (children between 6-years showed a 30 minutes decrease in total sleeptime (TST) in the fourth week compared to baseline, Effect size: .22), but different preparations and doses did not affect the result (after baseline, there was an 11–21-minute decrease in TSTfor the lower dose group and a 16–25-minute decrease in TST forthe higher dose group ($p < .05$, Effect Size: .10). There were no significant differences in TST changes between the lower and higher dose groups).

(continued)

Table 7. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Cockcroft et al. (2009)	Cross sectional	ADHD:23	69%/31%	(12 were on MPH, 11 medication naïve).	6.4–12.7 years	Parental questionnaire and the Wits Faces Sleepiness Scale. Limitations: Small sample size, no objective measure of sleep was used, no TD control group to assess if absence of pathology can also include daytime sleepiness.	To investigate whether treatment with methylphenidate had an effect on daytime sleepiness in children with ADHD and whether these changes could be noticed by parents and/or the children themselves.	There was a significant increase in perceived daytime sleepiness inthe medicated group ($p < .05$), but not in the un-medicated group, between 08:30 and 13:00. The parents of the un-medicated group perceived their children as having significantly higher levels of daytime sleepiness between the hours of 13:00 and 15:00 ($p < .05$) than the parents of the medicated group.
Mohammadpour et al. (2018)	Randomized control trial	ADHD: 62	74%/26%	The participants were not on psycho-stimulants until 4 weeks before the testing.	5–12 years	Conner's Parent Rating Scale-Revised, ADHD rating scale-IV, Weekly Parent Ratings of Evening and Morning Behavior (WPREMB), Serum levels, Anthropometric variables, dietary intake, physical activity, sun exposure, and side effects. Limitations: Low doses of vitamin D and short duration of supplementation.	The effect of two groups receiving either 2000IU vitamin D or placebo in addition to MPH for 8 weeks.	Evening symptoms and total score of WPREMB scale were significantly different at weeks 4 and 8 between the two groups8 ($p = .013$, .016, respectively), but no differences were found in symptoms by CPRS and ADHD-RS scales, however ADHD-RS total score showed significant differences between week 4 and 8 only within vitamin D group ($p = .040$).
Mohammadzadeh et al. (2019)	Clinical drug trial	ADHD:66	74%/26%	Not mentioned.	6–12 years	ADHD parents rating scale, demographic checklist, drug complication checklist. Limitations: Small sample size, gender imbalance, no measurement of blood levels of EPA and docosahexaenoic acid, duration of the study was 8 weeks, which was a short time	To study the efficacy between MPH with omega-3 group and MPH with placebo for 8 weeks.	The results showed no significant difference between the MPH with omega-3 group and MPH with placebo group based on the Parents ADHD Rating Scale between week 0 and week 8 ($p = .692$), Inattention ($p \geq .48$)and hyperactivity/impulsivity ($p \geq .80$) subscale scores.
Sonuga-Barke et al. (2009)	Randomized control trial	ADHD:184	74%/26%	99 children were on Concerta three times a day and 42 were on Equasym XL/Metadate CD two times a day.	6–12 years	Barkley Stimulant Side Effect Rating Scale (BSSERS). Limitations: Participants already being successfully treated with MPH so severe adverse events unlikely to be seen in study, trial underpowered for detecting rare events that could be severe, adverse events, measures of adverse events were derived only from parent ratings and not from direct observations of behavior.	Equasym XL/Metadate CD, Concerta, and placebo (PLA).	Treatment effects were seen only for emotionality (which improved $p = .002$) and sleep and appetite (which worsened ($p = .001$).

(continued)

Authors/ publication year	Study design	Participant characteristics				Primary measures, limitations and biases	Objective	Summary of main results
		Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age			Interventions/comparisons/ outcomes
Zarinara et al. (2010)	Randomized controlled trial	ADHD: 38 (MPH:19, Venlafaxine: 19)	71%/29%	Not mentioned.	6–12 years	ADHD teacher and parent rating, complications and side effects record. Limitations: Lack of placebo group, use of only ADHD Rating Scale for measuring outcome, relatively small number of participants.	Randomly assigned to receive capsules of venlafaxine at doses of 50–75 mg/day or methylphenidate at a dose of 20–30 mg/ day for a 6-week.	Venlafaxine comparable to methylphenidate, improved symptoms of ADHD (significant effect of both protocols on Parent ADHD Rating Scale scores ($p < .001$), differences between two protocols were not significant at the endpoint ($p = .17$) but venlafaxine tolerability was superior with less headaches (57.89% vs. 15.78%, $p = .05$) and insomnia (52.63% vs. 10.52%, $p = .01$).
Ironside et al. (2010)	Placebo controlled medication trial	ADHD:16	75%/25%	Medication naïve.	6–12 years	Actigraphy, Sleep diary. Limitations: Small sample size, medication administered at 4:00pm afternoon, failed to metabolize by night causing sleep onset problems, this could be exploredby having varying timings for drug administration.	To examine the effect of 3-week MPH- Immediate Release trial on 24 hour motor activity profile.	The children demonstrated significant increases in motor activity during the sleep-onset latency period (Placebo-23.63 (9.25), low dose MPH- 37.23 (11.11), High dose MPH- 37.60 (12.62), $p < .001$) and significant reduction in relative circadian amplitude (from a relative amplitude of 92.55 during the placebo condition to 84.16 on the low dose and 84.47 on the moderate dose ($p = .002$) and a phase-delay in the timing of the daily rhythm ($p = .03$).
Buchhorn et al. (2012)	Case control	ADHD: 23, Control: 19	82%/18%	11 children with ADHD received MPH medication	8–12 years	Electro-cardiogram recordings. Limitations: Retrospective study, (preselection could imply that sample represents a risk subsample of children with ADHD). Additionally, uniform ADHD diagnostic study manual not applied, small group sizes.	Comparing the effect of MPH on Heart Rate Variability.	Compared to healthy controls, the ADHD children with and without MPH treatment showed significantly higher mean heart rates (ADHD without MPH: 94.3 ± 2.2; ADHD with MPH: 90.5 ± 1.8, controls: 84.7 ± 1.8, both ts >2.2, ps <.033), while the ADHD groups (MPH & no medication) (t (29) = 1.7, $p = .107$).

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Table 7. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
*Wang et al. (2017)	Cross sectional	ADHD: 50, Control: 50	80%/20% RT,	Not currently medicated.	6–12 years	SNAP-IV, CBCL, CPT, ADHD- Saliva Cortisol test. Limitations: Saliva samples collected from patients in hospital but from healthy controls in school, no measurements of cortisol increment levels were made after baseline and during first month of treatment, waking time of participants was not precisely identified, patients with ODD or conduct disorder excluded.	To determine the trend in cortisol levels in children with ADHD and controls.	The cortisol levels of ADHD patients increased significantly after 1 month of MPH treatment (significantly higher than those at pre-treatment; mean difference = .11, p = .046). before decreasing to an intermediate level, but were significantly positively correlated with neuropsychological performance (salivary Cortisol was found tobe independently and significantlycorrelated with impulse control (=−.006, p=.003).
Slama et al. (2015)	Randomized controlled trial.	ADHD:36 (equally distributed between groups (placebo and osmotic-release oral system methylphenidate), Control: 40	100%/0%	The usual medication was replaced by OROS-MPH or placebo for 3 days and the subjects were tested on the third day, 8 to 10 hoursafter intake (at the endof the afternoon).	7–12 years	Continuous Performance Test-X [CPT-X], continuous performance test-AX [CPT-AX]), counting Stroop.Limitations: Study did not use computerized Stroop task, performance might have been influenced by presenceof stimuli in area surrounding target, rating by observer may also result in relatively inaccuratescoring, only boys were tested.	A double-blind, randomized, placebo-controlled study investigating effect of OROS MPH.	Participants responded faster in CPT-AX (542 ms) than in the CPT-X (654 ms), p<.001, Reaction time latencies were influenced by treatment, p=.026 and ADHD children with OROS-MPH responded faster (559 ms) than ADHD children with placebo (638 ms, p=.019).
Faraone et al. (2009)	Randomized controlled trial.	ADHD:268 (81 received placebo,98 received MTS, and 89 received OROS)	Not mentioned.	Participants abstained from any CNS active medication for 30 days prior to the study.	6–12 years	CSHQ, K–SADS–PL, K-BIT (intelligence). Limitations: For CSHQ 95th percentile and aboveconsidered to be of value 65/ above, and only 1 participant gotthat score (with the highest MPHdose), which might not be actualrepresentation of high, rating scales of sleep problems may lack validity as compared with findings from sleep laboratories (using PSG, Actigraphy).	To examine indices of sleep behavior (including severity and frequency of each type of sleep problem) among ADHD children treated with either once-daily oral methylphenidate (osmotic-release oral system, OROS), the methylphenidate transdermal system (MTS), or placebo.	The main predictor of sleep problems was severity of pre-existing sleep problems(= .267; z=9.68; p<.001), whereas no significant linear effect of methylphenidate dosagewas observed overall (p = .135), and this lack of effect was uniform across the two differentmethylphenidate preparations (OROS & MTS) as evidenced by the non-significant interaction of dose and treatment (p= .852).

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Table 7. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Ashkenasi (2011)	Retrospective randomized trial	ADHD: 26	73%/27%	All participants were allowed to be on study medication only.	6–12 years	Sleep diary, Attention Deficit Hyperactivity Disorder Rating Scale-IV (ADHD-RS) and Connor's Global Impression-Parent (CGI-PS). Limitations: Small sample size did not permit closely examining individual signs from ADHD-RS-IV/CGI-Parent Scale (whether longer patch times help with symptom),reliance on caregiver reports of patch wear times and sleep parameters.	To study the effect of ransdermal MPH patch wear time (9hours, 10 hours, 11 hours, and 12 hours) and randomization day (Monday, Tuesday, Wednesday, and Thursday) on sleep parameters.	Sleep parameters were not adversely affected by longer methylphenidate transdermal system patch wear times sleep latency ($p = .558$) or total sleep time ($p = .382$), however marginally significant trend toward better sleep quality at longer patch wear times ($F(1,341) = 3.60$, $p = .059$) was observed.
Findling et al. (2009)	Randomized controlled trial	ADHD: 327	64%/36%	Participants were not any (non-study related) medication during the study.	6–12 years	Adverse events (AEs), physical examinations, vital signs, electrocardiograms, laboratorytests, the Children's Sleep Habits Questionnaire, and the occurrence of application-site reactions. Limitations: MTS tolerability/effectiveness assessedusing open-label design, lacking blinding, susceptible to observer bias, lack of a placebo arm, results of long-term, open-label studies may be biased, as subjects remaining in study may continue to have improvements in ADHD symptoms, majority of participants were white males.	To assess the 12-month tolerabilityof MTS (MPH transdermal system)in children with ADHD.	81.3% reported adverse effects,of which 98.3% were mild or moderate in severity. Long-term tolerability of transdermal MPH found no apparent overall effecton sleep behavior, however the participants 8.9% incidence of Insomnia.
Chin et al. (2018)	Case control study	ADHD: 71, Control: 30	76%/24%	Participants were not medicated for ADHD in the past 6 months.	6–12 years	Polysomnography (PSG), Paediatric Sleep Questionnaire (PSQ). Limitations: One-night PSG at baseline and at 6 monthsfollow up, possible variability in measurements from night to night.	To study the effect of MPH treatment on sleep problems.	For the ADHD group after 6 months' treatment PSG data showed significantly increased total sleep time ($p = .005$) and decreased periodic limb movement index (PLMI) ($p = .031$) after 6-month MPH treatment, significant increases in AHI ($p = .012$) and hypopnea counts ($p = .008$). For the PSQ data, significantly decreased ratesof PLMD ($p = .029$) and sleep onset latency ($p = .021$) were shown.

Table 7. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Morash-Conway et al. (2017)	Placebo controlled randomized trial	ADHD:21	80%/20%	Medication naïve.	6–12 years	PSG and cognitive assessment. Limitations: Need for larger/ varied sample size would allow more in-depth analyses, computerized test used (mightnot represent actual daily functioning), so classroom observation would have been apt, cognitive processes related to long-term academic and functional outcomes not explored.	4-week blinded placebo-controlled randomized trial of long-acting MPH.	Long-acting stimulant medication was found to be an effective treatment for enhancing alerting attention (p = .003 with tone), (p < .001, without tone) executive attention (p < .001), working memory (p = .032), and academic productivity (p = .033), but resulted in poorer sleep (children were sleeping on average 40 minutes less while taking medication).
Ricketts et al. (2018)	Cross sectional intervention study	ADHD:576 (Behavioral treatment (n = 144), Medication management (n = 143) Combined treatment (n = 144) Community care (n = 145).	80%/20%	175 on stimulant medication at study onset	7–9 years	SNAP-IV, CBCL, Children's Depression Inventory (CDI), Multidimensional Anxiety Scale for Children (MASC). Limitations: Sleep-related items in CBCL used do not compose well-validated sleep measure, homogenous sample (ADHD subtype- ADHD-Combined type), age range restricted to young children limiting extension of conclusions to older children/ adolescents, lower average daily MPH dose in community care may have confounded group effects.	The effect of MPH, behavior therapy and their combination, community care on sleep measures.	There was no significant effects of treatment assignment on baseline sleep problems score for medication (z = −.37, p = .71), behavioral treatment (z = −.74, p = .46), or combined treatment (z = .44, p = .85) relative to community care and also no significant simple effects of treatment assignment on posttreatment sleep problems score for medication (z = −1.11, p = .27) or behavioral treatment (z = −1.17, p = .24) relative to community care, however, combined treatment on sleep problems relative to community care (z = −3.02, p = .003).
Kim (2010)	Cross sectional intervention study	ADHD: 24	91%/9%	Stimulant naïve.	6–12 years	PSG, CSHQ, Barkley Adverse Effects Ratings Scale, CBCL, Clinical Global Impression (CGI) scale- Improvement, State Trait Anxiety Inventory, Yale Global Tick Severity Scale, K-ARS, K-SADS-PL-Korean version, Children's Depression Inventory (CDI). Limitations: Small sample size, open-label study (OROS MPH effectiveness could be overestimated and evaluation of adverse effects and tolerability limited by not having placebo comparator.	To study the effect of MPH-OROS extended release on sleep architecture measured through PSG & CSHQ.	After OROS MPH administration, percentage of stage 2 sleep was increased (p = .024), number of awakenings was decreased (p = .047) and relative to baseline, parasomnias scale's score on the CSHQ were decreased (p = .033), Sleep Onset. Latency was increased in children with subjective sleep difficulties (Effect size = .226). Bedtime Resistance and Sleep Onset Delay in Children's Sleep Habits Questionnaire were also increased for OROS MPH in individuals with sleep complaints (Effect size = .185; Effect size = .248 respectively).

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Table 7. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Kim et al. (2011)	Cross sectional intervention study	ADHD: 102	92%/82%	All participants were on a daily dose of MPH for 4 weeks, and stable dose of MPH for 3 weeks before the study.	6–12 years	Inattentive/Overactive and Oppositional/Defiant subscales of the IOWA Conner's Rating Scale, Clinical Global Impression (CGI) scale, parents/caregiversrated sleep quality using a 4-point scale (poor, fair, good, excellent) during all visits. Limitations: Switching process resulted higher daily MPH doses although differences were not large, groups receiving twice a day vs. three times a day MPH-IR regimens not separately compared, investigators-participants not blind treatment conditions, no control group.	To evaluate the efficacy and safety of OROS-MPH among children with ADHD who had been previously treated MPH-IR.	Parent/caregiver ratings on the Conners subscale, showed statistically significant improvement after 4 weeks of treatment with OROS- MPH ($p<.001$). However, the teachers' ratings on the same subscale did not reflect any significant improvemen There were no statistically significant changes in sleep related adverse effects for both preparations of MPH.
Pelham et al. (2011)	Randomized controlled trial	ADHD: 9	100%/0%	All participants were receiving a stable dose of IR MPH before enrolment, but none had previously been treated with Extended release stimulants.	6–9 years	Twelve hourly assessments of classroom behavior and productivity were completed with efficacy measures of rule violations, math correct, Inattention/over activity teacher rating/oppositional defiant teacher rating. Limitations: Small sample size, all male, 80% comorbid ODD/CD, MTS applied for 24 consecutive hour exceeding FDA-approved wear time of 9 hour, all participants previously stabilized on MPH (cannot generalize the tolerability findings to stimulant naïve children).	Efficacy and tolerability of MPH- transdermal formulation (MTS) against Immediate Release- MPH (IR-MPH) and placebo in a 12-hour analog classroom setting.	MTS demonstrates comparable efficacy (for rule violations ($p = .01$), math correct responses ($p<.001$, only for MPH), inattention ($p=.02$)and oppositional defiance ($p=.02$) ratings) and tolerability (non-significant differences in adverse reactions) to TID IR MPH.

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Table 7. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Pliszka et al. (2017)	Randomized controlled trial	ADHD: 163 (Delayed Release DR/Extended Release ER-MPH, $n=81$; placebo, $n=80$)	70.2%/29.8%	Stimulants, clonidine, and guanfacine required a ≥72-hour washout, and any other medication to treat ADHD required a ≥7-day washout before randomization.	6–12 years	ADHD rating scale-IV (ADHD-RS-IV), Before-School Functioning Questionnaire (BSFQ), Parent Rating of Evening and Morning Behavior-Revised, morning (PREMB-R AM) and evening (PREMB-R PM). Limitations: Short study duration limits abilityto extrapolate findings over long term, participants aged 6–12 years, therefore, applicabilityof findings to other age groups unknown, enrolled participants previously shown partial responseto MPH (therefore, response and safety profiles in MPH-naïve patients may be different than those achieved in this study).	3-week trial of delayed-release and extended-release methylphenidate (DR/ER-MPH) formulation.	DR/ER-MPH was generally well tolerated and demonstrated significant improvements versus placebo in ADHD symptoms (after 1 ($p<.001$) and 2 weeks of treatment ($p=.002$) and at-home functional impairments (early morning, late afternoon and evening) (PREMB-R, $p<.001$)and PREMB-R PM ($p=.002$).
Giblin and Strobel (2011)	Randomized controlled trial	ADHD: 24 (3, 11, 2, 8 for the 30 mg/d, 50 mg/d, 70 mg/d, and placebo groups, respectively)	41.6%/58.4%	21 children had previously been on medication.	6–12 years	PSG, Actigraphy, CSHQ, Sleep hygiene/ sleep schedule inctructions, ADHD-RS IV, Clinical Global Impression-Severity Scale (CGI-Impressions), Conner's Parent Rating Scale-Revised: Short Form. Limitations: Effect of LDX treatment assessed in relatively small patient sample, comorbid psychiatric diseases excluded, limiting generalization of results to broader population of ADHD, PSG data may in part be explained by habituation sleep laboratory setting.	3 doses of Lisdexamfetamine Dimesylate (LDX) (30, 50, and 70 mg/ day) over a 10-week period	Number of awakenings as measured by PSG data was significantly decreased from 7.9±4.5 to 3.3±4.3 in the LDX-treated group when compared to baseline ($p<.0001$), howeverno difference was seen for totalsleep time or Wake after sleep onset measures. No significant difference was seen for actigraphdata or CSHQ reports.
Wigal et al. (2009)	Randomized controlled trial	ADHD; 129 (30 mg/d- 58, 50 mg/d- 50, 70 mg/d- 21)	76%/24%	Washout period of 7 days before start of study for participants if applicable	6–12 years	SKAMP-D, Permanent Product Measure of Performance (PERMP), CGI, ADHD-RS-IV, blood pressure, ECG, clinical laboratory test, treatment emergent adverse effects screening. Limitations: Short treatment duration and assessment phases may underestimate TEAEs, subjects with severe comorbid psychiatric conditions excluded, unblinded design- thereby subject to biases, no measurements beyond13 hours post dose captured, lack of subjects with inattentive type ADHD, under-representation of minority populations.	4-week dose-optimization of LDX (30, 50, 70 mg/day	Treatment emergent adverse effect (insomnia-27%).

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Table 7. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Wigal et al. (2012)	Intervention study	ADHD: 27	77.8%/22.2%	Stimulant washout period of 7 days before start of study for participants (14) if applicable	6–12 years	CGI, ADHD-RS-IV, treatment emergent adverse effects screening. Limitations: Small sample size, few female subjects,no randomization to placebo within exposure based groups toallow comparison to potential placebo effects, no inclusion of untreated group.	LDX, initiated at 30 mg, was dose titrated in 20 mg increments to a possible 70 mg over 4–5 weeks, and its effect was studied on the initial onset of efficacy when compared to placebo.	The stimulant naïve group as wellas the previous-exposure group reported trouble sleeping and stomach pain with a greater incidence for stimulant naïve subjects ($p = .004$, and $p = .0034$, respectively), hyperfocus ($p = .025$) was only seen in the stimulant naive subjects, howeveronly previous-exposure subjects experienced dizziness ($p = .037$).
Rugino (2018)	Randomized controlled trial	ADHD: 29	58%/42%	12 participants were on stimulant medication before beginning of study, and 6 out of them had a stimulant washout period before commencing study.	6–12 years	Polysomno-gram, a CSHQ, an ADHD-RS, ADHD CGI-I, a sleep CGI-I, vital signs, growth parameters, physical examination, detailed interval medical history, ECG, and laboratory investigations. Limitations: Small sample size, short treatment time, single PSG may not represent effect on sleep at home over extended time, data cannot be generalized to children administered GXR in the evening, cannot be generalized to ADHD population without primary sleep disorder, unequal sample sizes at baseline and termination not explored.	Guanfacine extended release (GXR) administration.	Although none of the PSG measured sleep parameters demonstrated difference between GXR and placebo, ADHD Rating Scale-IV combinedscores for guanfacine extended release and placebo groups at baseline and at endpoint showed difference ($p < .001$, effect size: .41).
Young et al. (2014)	Randomized controlled trial	ADHD: 333 (GXR a.m., $n = 107$; GXR p.m., $n = 114$; placebo, $n = 112$)	70%30%	Not mentioned.	6–12 years	Paediatric Daytime Sleepiness Scale (PDSS), Conner's Parents Rating Scale – Revised (CPRS-R), Adverse effects, laboratory tests, physical examinations. Limitations: CPRS–R:S modified to evaluate ADHD-symptoms at several time points throughout the day, which may limit interpretation results, study was not powered to formally assess differences between the a.m. and p.m. cohorts, the PDSS has not demonstrated correlation with objective measures such as PSG, as a self-report measure, results may be subject to rater bias.	Once-daily Guanfacine extended release (GXR) monotherapy administered either in the morning or evening.	Subjects receiving GXR showed significantly greater improvements from baseline compared with placebo, regardless of time of administration ($p < .003$ vs. placebo across all subscales for GXR a.m. and GXR p.m.) Effect sizes were similar for both morning and evening GXR administration (.71 and .62, respectively). The most frequently reported AEs (reported in >10%of subjects) in the GXR groups were somnolence, headache, sedation, upper abdominal pain, and fatigue.

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Table 7. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Connor et al. (2010)	Randomized controlled trial	ADHD: 217	68.7%/38.3%	Participants were not on any medication.	6–12 years	Conner's Parents Rating Scale – Revised (CPRS-R), ADHD-RS-IV, ECG and laboratory tests. Limitations: Subjects co-existing psychiatric conditions excluded, study duration only 8 weeks, study did not include teacher ratings to assess behavior in classroom, study not designed to investigate effects of guanfacine XR on oppositional symptoms.	Guanfacine extended release (1–4 mg/ day) or placebo for 9 weeks to examine its safety and efficacy outcome.	Reduction in ADHD-RS-IV total score from baseline to endpoint in Guanfacine-treated group compared with the placebo group (23.8 vs. 11.5, respectively; $p<.001$; effect size = .92), percentage reduction from baseline to endpoint in CPRS-scores for oppositional subscale and ADHD-RS-IV total scores indicated that the decrease between the two was highly correlated ($r=.74$). Most commonly reported, treatment-emergent AEs in the guanfacine XR group was somnolence (50.7%).
Montoya et al. (2009)	Randomized controlled trial	ADHD: 113 (children group)	79.5%/20.5%	Medication naïve.	6–12 years	Conner's Parents Rating Scale – Revised (CPRS-R), ADHD-RS-IV, ADHD Clinical Global Impression on severity (CGI-ADHD-S). Limitations: Small sample size (less statistical power), due to short duration, effect size on symptoms ratings beyond week 12, the development of tolerance, the occurrence of hepatic disorders or long term consequences of vital signs changes, could not be addressed, teacher ratings not obtained, neuropsychological tests not included.	Atomoxetine or placebo, respectively, for 12 weeks to examine its safety and efficacy.	Treatment-related adverse events were significantly more frequent with atomoxetine (65.0%) than with placebo (37.3%), the most frequent being decreased appetite ($p=.006$) and somnolence ($p=.002$).
Wehmeier et al. (2011)	Randomized controlled trial	ADHD: 105 (ATX group: $n=54$; placebo group: $n=51$)	77.6%/32.4%	Atomoxetine naïve, not currently treated with other psychotropic drugs.	6–12 years	Computerized performance test (CPT), infra-red motion tracking device, Weekly Ratings of Morning. Limitations: Relatively short duration of observation period, CPT tool not gold standard tool for assessing ADHD symptom severity, be the close oversight of the patient bythe physician may have influenced Clinical Rating Scale scores.	Atomoxetine (ATX) dose of 1.2 mg/kg/day for 8 weeks' effect on neuro-cognitive performance.	The WREMB-R total score (effect size − 1.00) and the sub scores (late noon and evening subscore-effect size 1.02 & Difficulty falling asleep- effect size- .62) showed statistically significant differences between the treatment groupsat week 8 ($p<.001$) ATX was significantly superior to placebo in reducing ADHD symptom severity as measured by ADHD-RS (effect size- 1.30) and CGI-S scores (effect size − 1.11).

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Table 7. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
England et al. (2011)	Randomized controlled trial	ADHD, ADHD+Restless Leg syndrome: 29	68%/32%	All participants were CNS active medication naïve.	7–12 years	PSG, Conner's rating scales and neuro-psychometric testingat baseline and endpoint. Limitations: Study did not directlytest impact of improvement of RLS symptoms on quality of life, small sample size.	Carbidopa/L-DOPA or placebo for 8 to13 weeks to see if ADHD symptoms improve differentiallyin children with and without RLS/PLMS.	ADHD was more severe in children without RLS/PLMS than in children with RLS/PLMS (p = .006), however L-Dopa significantly improved RLS/PLMS (p=.007) but not ADHD.
Ferri et al. (2013)	Case control study with second phase of randomized controlled trial with ADHD patients	ADHD: 18, Control: 17	61%/49%	Participants were not on medication.	7–12 years	PSG, scoring of leg movements. Limitations: Lack of comparison group (children with RLS but not ADHD); no data on iron status, results more relevant (children with ADHD accompanied by sleep disturbance than for ADHD in general).	To assess the effect of Carbidopa 25 mg/*L*-DOPA 100 mg CR per tablet on changes on the leg movement (LMs) time structure in ADHD children.	LMs during sleep in children with ADHD do not show a highly periodic character and are not considerably modified by *L*-DOPA treatment.
Hoebert et al. (2009)	Randomized controlled trial	ADHD+Sleep Onset Insomnia: 93	74.5%/26.5%	Participants were not on stimulant medication at the beginning of the study. Information about other medicationuse not mentioned.	6–12 years	Parent questionnaire with combination of multiple choice, numeric, open ended and scaled questions, 19 in total. Limitations:Parents reporting adverse events from Melatonin not carefully interviewed, co-medication not reported, lack of measures to assess long-term effects of melatonin treatment on pubertaldevelopment and fertility, lack ofcontrol treatment.	Longitudinal follow up (average 3.7 years) study of Melatonin use and discontinuing.	Melatonin is an effective therapy for CSOI in children with ADHD, but does not reduce ADHD symptoms themselves 67 children temporarily discontinued Melatonin and 22%discontinued completely. For those discontinued completely- Dim Light Melatonin Onset (DLMO) for the discontinuing children when compared to restof subjects was not different (p=.413, effect size=.09). For those who discontinued temporarily- effects in: No change of sleeping pattern (1.5%). Delay of sleep onset time (92.3%). Delay of wake uptime (30.8%). Changing daytimebehavior (29.2%) was observed when compared to the rest of the subjects, who did not discontinue (p=.06).

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Table 7. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Gender (male%/ female%)	Medication use	Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Masi et al. (2019)	Naturalistic treatment with MPH	ADHD: 42 children under 12 years	93%/7%	Participants were on MPH medication.	6–12 years	K-SADS-PL, Clinical Global Impression Severity (CGI-S), Conner's Parents and teacher rating scale. Limitations: CGI-I used as outcome measure, not measure of sleep disorder severity and improvement, lack of previously validated questionnaires, sleep diary and actigraphy, limits reliability of results, lack of specific information about sleep habits before starting MPH.	MPH mean dosage average 33.5 mg/ day, melatonin on sleep (mean dosage average 1.85 mg/d) for 4 weeks, to gage effectiveness.	Melatonin is effective (clinical severity for the CGI-S reducedto 2.13 ± 1.05 at follow up from 3.41 ± .70 at baseline ($p < .001$) treatment, irrespective of gender, age and comorbidities, for ADHD children with sleep problems.
Blumer et al. (2009)	Randomized controlled trial	ADHD: 111 (6–11 years)	Not mentioned.	Nonhypnotic medications were used for sleep by 41 patients in the zolpidem group (Clonidine) and 23 patients in the placebo group (Antihistamines and other drugs with drowsiness as a side effect).	6–11 years	PSG, Clinical Global Impression scale (CGI), Peadiatric Daytime Sleepiness Scale (PDSS), ADHD-RS-IV, Conner's Continuous performance test- II (CPT-II), adverse effects assessment. Limitations: Potential for drug interactions not noted, responses to zolpidem for children receiving different medications for insomnia and/ or ADHD before the study were not evaluated.	To evaluate the hypnotic efficacy of Zolpidem 0.25 mg/ kg per day among ADHD children.	Zolpidem at a dose of 0.25 mg/ kg per day failed to reduce the latency to persistent sleep on PSG recordings (20.28 vs. 21.27 minutes).
Lyon et al. (2011)	Randomized controlled trial	ADHD:98	100%/0%	27 on stimulant medication during study (13-treatment group and 14-placebo group).	8–12 years	Peadiatric Sleep Questionnaire (PSQ), Actigraph. Limitations: Only male participants, no othersocial-emotional functioning scale used, therefore behavioraloutcomes not examined.	L- theanine 400 mg daily at breakfast and after school on sleep quality.	Increased percent of time spent in restful sleep in L-theanine compared to placebo group ($p <$ .05), fewer bouts of nocturnal activity in L-theanine compared to placebo group, $p < .05$, lower number of minutesspent awake after onset of sleep in the L-theanine compared to the placebo group ($p < .058$).

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Table 7. (continued)

Authors/ publication year	Study design	Participant characteristics: Sample size and diagnosis	Participant characteristics: Gender (male%/ female%)	Participant characteristics: Medication use	Participant characteristics: Age	Primary measures, limitations and biases	Objective	Summary of main results: Interventions/comparisons/ outcomes
Blader et al. (2009)	Randomized controlled trial	ADHD: 27	77%/23%	16 children were on medication at enrolment	6–13 years	Retrospective-Modified-Overt Aggression-Scale, Child-Behavior Ckecklist (CBCL), K-SADS-PL, Conner's Global Index- parent version, Barkley Behavior and Adverse Events Questionnaire–Modified. Limitations: Small sample size.	Titration began with triphasic-release MPH preparation (Concerta) 90 mg/day or biphasically released MPH product (Metadate CD) daily dose 60 mg, concurrent psychosocial treatment-Community parent education program for 5 weeks, Divalproex extended-release once-daily preparation for 8 weeks to examine the effect of reducing aggressive behaviors.	The odds of remission with divalproex treatment were seven times greater than that with placebo, although a small sample size rendered the confidence interval (CI) for this estimate especially wide (odds ratio = 7.33, $p < .05$).
Newcorn et al. (2013)	Randomized controlled trial	ADHD: 332, GXR AM ($n = 107$), GXR PM ($n = 114$), or placebo ($n = 112$).	70%/30%	Not mentioned.	6–12 years	ADHD-RS-IV, Pediatric Daytime Sleepiness Scale, Medical Dictionary for Regulatory Activities (MedDRA). Limitations: Study was not adequately powered to detect small differences between GXR AM and GXR PM treatment arms, drug administration times limited to 2 time points: morning or evening, subjects not required to complete self-report or structured scale of AEs (caregiver ratings may be subject to underreporting, rater bias or halo effects), subject cohort consisted predominantly of white males.	8-week, double-blind, dose-optimization study for morning and evening Guanfacine administration.	Treatment-emergent adverse events were although mild or moderate in severity; the most common was somnolence (GXR all-active: 44.3%; GXR AM: 46.7%; GXR PM: 42.1%; placebo: 12.5%). Significant differences in ADHD-RS-IV total scores between GXR & placebo- Effect sizes were .77, .75, and .78 for the all-active, GXR AM, and GXR PM groups, respectively.

2.4 Discussion

The current review aimed at providing a comprehensive overview of the associations between sleep and circadian function with ADHD in children. The breadth of the topic and the need for the review was reflected in the large number of studies included.

For the subjective assessment of sleep in children with ADHD, 119 (out of the total 148) selected articles utilized subjective parental/caregiver reports of sleep, and these reports highlighted higher occurrence of bedtime resistance, sleep anxiety, sleep onset delay, sleep disordered breathing, day time sleepiness and a general trend of poorer sleep quality, duration and efficiency (Abou-Khadra et al., 2013; Akinci et al., 2015; Becker, Pfiffner, et al., 2016; Chiraphadhanakul et al., 2015; Gomes et al., 2014; Moreau et al., 2013; Scott et al., 2013). In assessing studies utilizing parental/caregiver reports of childrens' sleep, it is important to recognize various sources of potential bias in such reports and the bidirectional nature of the relationship between children's sleep and parental/caregiver wellbeing, and the consequent potential for altered subjective appraisal of children's sleep parameters. The relationship between parental stress and sleep problems in children with ADHD wherein children's sleep dysfunction causes a decrease in the parent's wellbeing and increased fatigue was noted in the review of Martin et al. (2019), and such effects may decrease parents' ability to implement more consistent/ effective behavioral and sleep management strategies for the child. As such, an important limitation for some of the reviewed articles is the absence of information about parental stress, presence of family psychiatric history, family's social-economic status or parent's education (Bergwerff et al., 2016; Bériault et al., 2018; Eyuboglu and Eyuboglu, 2018; Kwon et al., 2014; Matsuoka et al., 2014; Williams et al., 2016). Studies included in the current review also indicate that sleep problems in ADHD are associated with externalizing and internalizing comorbidities in the child and caregivers' own attitudes, sleep quality, lifestyle

trends and socio economic conditions (Bessey, Richards, et al., 2013; Lycett, Mensah, et al., 2014; Matsuoka et al., 2014; Sciberras et al., 2016, 2017). Further, it is clear that sleep in children with ADHD should be considered carefully to all aspects of the child's environment, and such relation- ships may be best studied through well-powered and care- fully constructed longitudinal studies. Keeping in mind our selection criteria, we found 15 studies that have used a longitudinal design out of the total 148 reviewed articles. However longitudinal studies also reported specific weaknesses such as missing data, significant drop out rate for participants, all measures not assessed during baseline and follow-up consistently and data assessed through older or previous editions of measures (Mulraney et al., 2017; Schmid et al., 2014; Soehner et al., 2019). Additionally, given the fact that subjective ratings do not always bring about a comprehensive account of sleep related concerns among ADHD children, qualitative analysis of reports from caregivers/clinicians may be explored to examine sleep in childhood ADHD. As such, there are no studies that have explored sleep problems in ADHD children through qualitative methods such as thematic analysis.

Considering the nature of measures employed in studies based on subjective accounts, our review found wide ranging and dominant use of a few standard tools such as the Child Sleep Health Questionnaire (CSHQ), Pittsburgh Sleep Quality Questionnaire and Childhood Sleep Disturbance Scale (CSDS) etc. Although some of these scales have individual sub-scales and a global measure of sleep disturbance, how parents understand the difference between items while rating them and how they understand their child's specific sleep problems should be considered, as should the lack of congruence with results from objective measures such as actigraphy (Akinci et al., 2015; Choi et al., 2010). Further, sleep questionnaires do not usually assess information regarding restless leg syndromes or breathing problems during sleep, unless the tool is built for assessing such concerns specifically. Hence, to reach more consistent and comprehensive set of results, studies exploring similar variables through both objective and

subjective measures is recommended. In our reviewed list of articles, there were 44 studies (out of the total 148) which utilized a combination of both subjectively reported and objectively measured sleep functions, thereby underlying the need for more such investigations.

We uncovered mixed evidence for greater subjectively reported sleep problems in ADHD hyperactivity and combined presentation, than the inattentive subtype (Eyuboglu and Eyuboglu, 2017; Grünwald and Schlarb, 2017; Hansen et al., 2011; Sciberras et al., 2016). Similar links between sleep problems and hyperactivity or combined subtypes have been reported for older adolescents (Chiang et al., 2010; Mayes et al., 2009). Interestingly, among the reviewed studies, an important limitation is the lack of ADHD sub- type-based recruitment of participants (for articles exploring the nature of sleep and its consequences for the ADHD child), leading to non-comparable number of children exhibiting ADHD-I, H or C presentations, thereby most studies generalizing the sleep problems for all subtypes. Further, Tsai et al. (2019) found that relative to inattentive subtype, childhood combined subtype was associated with higher risks of sleep disorders during adulthood.

Studies based on objective sleep measures reported shorter sleep duration, longer sleep latency, lower sleep efficiency, greater wakening after sleep onset and sleep fragmentation in ADHD (Lee et al., 2014; Miano et al., 2019; Moreau et al., 2013). However, such findings are not reported in all relevant studies, with a number of studies showing no difference between ADHD and TD children's sleep profiles (Bergwerff et al., 2016; Waldon et al., 2015; Wiebe et al., 2012). Such discrepancies may be explained by variations in actigraphic protocols applied (e.g., how long the actiwatch is worn for, is it worn during school days or free days, the analytic algorithms applied) as well as differences in study cohorts. Nonetheless, given the good tolerability of actigraphy and its suitability for application in the home setting, such approaches should be further encouraged in the future according to more standardized methodology (Smith

et al., 2018). Further, most studies using actigraphy reviewed had sample sizes of 50 children or less in case control design, indicating a need for larger studies with sufficient statistical power to investigate issues such as the impacts of comorbid behaviour disorders on sleep in children with ADHD as well as the impacts of environmental and family factors on sleep. Another important factor is the effect of the time of the year when the study has been conducted, (example Christmas (Langevin and Ramdé, 2012) or outside of school term-time) when the usual schedules of the child are disrupted due to social or familial events, or for specific days of the weekend or weekdays.

Some studies utilizing PSG report changes in sleep architecture in children with ADHD, including less time spent in REM, shorter REM sleep latency and lower frequency of eye movement during REM (Akinci et al., 2015; Díaz- Roman & Buela-Casal et al., 2019; Grissom et al., 2009; Gruber et al., 2009), although such findings are not ubiquitous (eg. Kirov et al., 2012, report greater REM duration in ADHD). For NREM features, lower periodic EEG activity (Cyclic Alternating Pattern, CAP) for stage 2 sleep was indicated along with higher 12 Hz frontal spindle power for ADHD children when compared to controls and its significant positive relationship with reaction time variability measuring attention (Akinci et al., 2015; De Dea et al., 2018; Grissom et al., 2009; Saito et al., 2019; Silvestri et al., 2009). Lower CAP rate was also found by Miano et al. (2006) in children with ADHD, perhaps indicating hyper-arousal during NREM sleep in these children. Increased topographical distribution of Slow Wave Activity (SWA) localized over the central regions for ADHD children has been reported (Miano et al., 2019; Ringli et al., 2013) and previous studies have found that SWA has an age dependent shift that runs through the posterior-anterior axis between the age of 2 years and adolescence (Kurth et al., 2010; Novelli et al., 2016). Therefore, higher concentration of SWA in the central region among the ADHD children may reflect the neurodevelopmental nature of ADHD. However, findings of sleep EEG changes were not ubiquitous; Příhodová et al. (2012)

reported no significant alteration in sleep REM or NREM parameters in ADHD. Small study cohort sizes and variations in study protocols (e.g., number of consecutive nights PSG recording, home of clinical research setting) may underpin such discrepancies. Another significant limitation for studies employing nocturnal polysomnography records is that they have done so for one night, thereby not controlling the first night effect, and studies which have used only sleep lab records and not for home environments might be subject to effects of a novel sleep environment on the sleep parameters measured (Galland et al., 2010; Miano et al., 2019; Silvestri et. al., 2009; Um et al., 2016). Further although studies have mentioned the washout periods for the child's ongoing ADHD medications, abstaining from the medication might influence the child's sleep which might be reflected in the records, and this significantly effects the total results, especially if the PSG is done for 1 night (Galland et al., 2010). It might prove beneficial to acknowledge the above lapses as EEG recordings during sleep have the potential to reveal important neurophysiological insights into ADHD and lead to understanding of how sleep changes may contribute to ADHD symptoms in children.

Our review of the current literature on circadian function in children with ADHD revealed a somewhat limited set of investigations, with significant variations in methodology and some inconsistent findings. For example, better ADHD clinical scores were associated with higher morning cortisol levels were indicated by some studies (Angeli et al., 2018; Wang et al., 2017) but not others (Imeraj et al., 2012; Buske- Kirschbaum et al., 2019). We uncovered only two investigations of melatonin rhythms in childhood ADHD, with inconsistent findings (Novokova et al., 2011; Paclt et al., 2011). Likewise, there was a low number of studies examining chronotype and/or diurnal preference in children with ADHD (Van der Heijden et al., 2018; Tarakçioğlu et al., 2018). For both of these studies subjective reports of chronotype were utilized which is not as accurate as the use of objective measures such as actigraphy, or assessing Dim Light Melatonin onset. Moreover, the studies in this section have used case-

control design thereby limiting inference regarding long-term influence of sleep/ADHD associated behaviors on chronotype, which would be possible through longitudinal investigations. Our review found only 11 studies investigating circadian functions in ADHD children (10 case-control and 1 longitudinal). This lack of studies is striking in the context of the more developed literature in circadian function in adult ADHD (Coogan and McGowan, 2017), and may reflect the perceived difficulties of examining circadian rhythms in children. Given that the circadian system is a key shaper of sleep/wake behavior, this is an area that clearly warrants further research in ADHD.

Considering consequences of sleep problems in children with ADHD, the reviewed studies revealed consistent associations between anxiety/depression symptoms, as well as wider range internalizing and externalizing comorbidities, with sleep in children with ADHD (Becker et al., 2018; Blunden et al., 2011; Lucas et al., 2017; Lycett et al., 2016; Mulraney et al., 2016, 2017; Tong et al., 2018); such associations have also been previously indicated in adults with ADHD (Oğuztürk et al., 2013). There were also associations between poorer executive-cognitive functions and sleep deficits consistently reported in children with ADHD (Cremone, Kurdziel, et al., 2017; Hansen et al., 2013; Moreau et al., 2013). Cognitive functions assessed through manual/machine aided neuropsychological tests and sleep measures revealedcross sectional as well as longitudinal associations between these in ADHD (Cremone et al., 2018; Gruber et al., 2011; Kidwell et al., 2017; Saito et al., 2019; Sciberras et al., 2015; Surrattet al., 2011; Zambrano-sánchez et al., 2013). For example, Kidwell et al. (2017) found longitudinal associations between sleep problems at age 3 and higher levels of inattention/hyperactivity in 4th grade predicted by higher executive functions deficits. When underlining the above associations, it is vital to acknowledge (not based on the reviewed studies) that also for younger children, sleep problems such as bedtime resistance, fragmented sleep and sleep onset insomnia in earlier

years are related to increased likelihood of developing ADHD like symptoms later (Gregory et al 2002; O'Callaghan et al 2010).

Further, sleep may be important for emotional regulation in ADHD. Cremone et al. (2018) hypothesized that positive attention biases may be associated with heightened reward sensitivity in children with ADHD, causing overreliance on (positive cues) rewards, which may contribute to behavioral manifestations for emotional dysregulation. These studies highlight the potential significance of impaired sleep for cognition and emotional regulation in children with ADHD. However, the above findings should be interpreted with caution, as for most of the cross sectional studies (Lycett, Mensah, et al., 2015; Lycett et al., 2016; Lucas et al., 2019; Moreau et al., 2013; Sciberras et al., 2015; Thomas et al., 2018), the recruited ADHD children (with comorbid sleep concerns) might have presented higher level of ADHD symptom severity for which they were on medication, which in turn might have had an influence on the measured sleep feature. Additionally, the paucity of longitudinal studies exploring the developmental relationship between sleep functions and cognitive/emotional functions among ADHD children (our review located 6 such studies in this section) must be taken into consideration for future research.

Given that sleep disturbances appear to be consistently associated with cognitive and emotional problems in children with ADHD, it might be expected that cognitive/ behavioral interventions that are designed to improve sleep may result in lessened ADHD symptoms. Behavioral sleep interventions improved caregiver rated sleep functions along with a proportion of sleep mediated improvements in ADHD symptoms, behavior and quality of life (Bériault et al., 2018; Hiscock et al., 2015; Papapdopoulos et al., 2019). However, we found that the evidence base for this area is underdeveloped (we found the above mentioned 3 studies exploring this field of intervention). Sleep trainings further brought about wide range of improvements in the child's sleep functions and related behaviors (Corkum et al., 2016;

Keshavarzi et al., 2014; Peppers et al., 2016). Sleep hygiene interventions that have directly or simultaneously targeted sleep in ADHD had a beneficial effect on children's emotional, behavioral and social performance (Dewald- Kaufmann et al., 2013; Weiss et al., 2006). However, there is an absence of studies employing chronotherapeutic techniques for ADHD children that might involve using environmental stimuli to influence their biological clock. Also we noted only 6 randomized controlled trials, most of which had sample sizes in the range of 20 to 60 patients, again indicating a need for a more systematic approach involving larger (potentially multi-site) studies.

When examining the literature on the effects of ADHD pharmacotherapy on sleep, we found that a substantial number of studies (14 out of the 42 in this section) assessed sleep as a secondary outcome (often via a single item rating). 17 out of 42 of the included studies examined the effects of MPH, and a number of papers reported dose- dependent associations with greater sleep complaints, later bed times, negative effects on wake up time and total sleep time, day time sleepiness and higher insomnia (Becker, Pfiffner, et al., 2016; Childress et al., 2009; Cockcroft et al., 2009; Lee et al., 2011, 2012; Sonuga-Barke et al., 2009). However, some studies reported no negative effects of MPH on sleep (Ashkenasi 2011; Findling et al., 2009) and a few studies reported positive outcomes for sleep of MPH (Chin et al., 2018; Morash-Conway et al., 2017; Ricketts et al., 2018). Seven studies explored the effect of individual MPH preparations on sleep in childhood ADHD, with results not clearly indicating a preference for either extended or immediate release preparations (Kim 2010; Kim et al., 2011; Pelham et al., 2011; Pliszka et al., 2017). There were few studies assessing the sleep impacts of non-stimulant medication in children with ADHD (such as Atomoxetine, Guanfacine and Divalproex). The inconsistencies noted for MPH may be a function of the rudimentary characterization of sleep applied in many of these studies and indicates a need for more systematic assessment of MPH and other less commonly applied non-stimulant treatments on

sleep in children.

Manifesto for Future Research in Sleep and childhood ADHD

Drawing together the points highlighted above, we present a manifesto for future research on sleep in children with ADHD. The first is that as sleep is a complex phenomenon with multiple phases that can be measured in multiple ways (each approach with important advantages and disadvantages) and fulfills multiple functions, the assessment of sleep in ADHD studies should be comprehensive and multifaceted. Such approaches should incorporate objective measures such as actigraphy and PSG in parallel with subjective measures such as parental report, and standardized protocols be applied when such consensus processes are available. Studies should be sufficiently well powered to allow for specified sub-group analysis (e.g., of ADHD sub- types). Secondly, proving causal relationships between sleep problems and functional outcomes in ADHD may not be achievable, rather a pragmatic approach of clinical utility may be adopted; that is to say the primary aim should be to develop and deploy effective interventions and further develop fundamental knowledge of the etiological and symptomatological profile of ADHD. There has been some interest recently in attempting to solve the "chicken and egg" question of sleep disturbance and ADHD; does one lead to the other, and if such in which order? (Bijlenga et al., 2019; Raman and Coogan, 2019). However, this may be a distinction that is not meaningful; for example, if sleep disturbance is part of the sytmptomatic profile of ADHD that manifests earlier than other symptoms during the developmental time course, then ascribing sleep changes as causal factors in the development of ADHD will not be justified. Future studies may examine the role of sleep parameters as state marker in ADHD during successful and unsuccessful treatment to hint at the relationship between sleep and the "classic" domains of inattention, hyperactivity and impulsivity. Further, we must consider whether there are generalized sleep disturbances associated with neuropsychiatric disorders, as whether there are specific features such as

delayed sleep timing or sleep maintenance problems that are more strongly associated with specific disorders such as ADHD (which has been argued to be the case in adult ADHD; Coogan and McGowan, 2017).

Thirdly, it should be borne in mind that mitigation of sleep problems, in and of themselves, may represent highly worthwhile goals, even if they are not accompanied by significant impacts on ADHD scores (e.g., by lessening sleep impacts in caregivers; Sacco et al., 2018). Fourthly, research should be directed to seemingly obvious questions relating to everyday clinical practice; an example of such an issue is whether time of dosing of different MPH formulations impacts sleep and ADHD symptoms differentially, as animal experiments indicate that this may be the case (Antle et al., 2012; Baird et al., 2013). Likewise, does time-of-day of testing on neuropsychological batteries impact on results in a clinically significant way, as is indicated in adults (Korman et al., 2019). Fifthly, when sleep behavioral interventions in ADHD are trialed they should be done so as blinded placebo controlled RCTs in multi-site studies to allow for sufficient statistical power; the literature as it is currently comprised is dominated by small, under-powered case-control studies that may pro- vide tantalizing indications of promise and/or causal relationships, but are not useful in guiding clinical practice unless they are built on by larger studies. Lastly, majority of the studies in our review had lesser number of female participants as compared to males, thereby significantly limiting generalizability of findings to females. Keeping in mind the gender based variations in both macro and micro structure of sleep (Acebo et al., 1996; Sadeh et al., 2000), circadian rhythm markers (Boivin et al., 2016; Cain et al., 2010; Duffy et al., 2011; Santhi et al., 2016) and even the ADHD clinical pictures (Biederman et al., 2002), it is indeed indicative that the effect each variable has on the other might be based on such differences. Therefore, studies investigating sleep properties among ADHD children are recommended to have comparable number of female and male participants, where gender-based findings are discussed.

Conclusion

We have conducted the first comprehensive systematic review of sleep in children with ADHD, examining studies involving −42,000 children. Our review highlights that reports of disturbed sleep in children with ADHD are common, that such disturbances may contribute to cognitive and emotional impairments and may be tractable through behavioral and cognitive sleep interventions. We have identified several important weaknesses and knowledge gaps in the literature and have laid out some points to be considered in the design and implementation of future studies of sleep in children with ADHD.

2.5 An update of the literature as of January 2023

Our systematic review (submitted for publication in 2020 and published in 2021), included studies published between 2009 and 2019. To incorporate an updated record of the literature, this chapter includes an additional section recording studies published between 1st January 2020 and January 30th, 2023, in the next section.

Section 2.5

Table 2.8 Updated research studies of sleep in childhood ADHD published between January 2020 – January 2023

Summary of studies focussing on subjective assessment of sleep in ADHD							
Authors/publication year	**Study Design**	**Participant characteristics**				**Objective**	**Summary of main results**
		Sample size and diagnosis	**Gender (male%/female %)**	**Medication use**	**Age**		**Interventions/Comparisons /Outcomes**
Bruni et al. 2021	Cross sectional	Total sample = 992 (out of which, Children = 528), All diagnosed with ADHD	441 boys, 87 girls	-	5-11 years	To examine the impact of home confinement because of COVID-19 pandemic on the sleep patterns of children with ADHD.	59.3% of children reported changes in bedtime, increase in number of children going to bed after 11 pm, 19.9% to 22 % slept less than they did before lockdown, but 21.4 – 27.4 % slept more. Bedtime delay and decreased sleep duration associated with increased screen time.
Gosling et al 2023	Longitudinal	N = 1055	-	-	Parents interviewed at 9, 13 and 18 years	Using random-intercept cross-lagged panel models to assess the directionality of the association of ADHD symptoms and sleep from childhood to early adulthood	Parent-reported sleep disturbances at age 13 years predicted increased ADHD symptoms 5 years later, and for inattentive symptoms, ADHD symptoms at age of 9 predicted increased sleep disturbances 4 years later.
Joseph et al. 2022	Case control	ADHD = 40, TDC group = 40	35 boys, 5 girls	ADHD group medication naive	6-12 years	To examine sleep disturbances in children with ADHD compared to their typically developing peers after controlling for moderating variables (age, sex, medication status,	65% of children with ADHD had a sleep disorder, as compared to 17% of controls. The ADHD group reported more sleep disturbances and disorders, both on subjective measures and objective measures.

						body mass index, and psychiatric and medical comorbidities).	
Harris et al. 2022	Qualitative study	21 parents	Mothers = 16 Fathers = 5 Boys = 11 Girls = 8	-	6-13 years (child's age), Parent age-32-48	To explore parents' experiences of direct and indirect implications of sleep quality on the health of children with ADHD.	Parents experienced that sleep influenced their children's abilities to control emotional behaviour related to ADHD and to manage everyday life. Sleep also had an impact on the children's well-being, in relation to both vitality and self-esteem.
Melegari et al 2023	Cross sectional	528 ADHD children	441 boys 87 girls	441 on ADHD medications prior to lockdown	5-18 years	To examine how changes in sleep patterns and sleep problems occurring between the pre-pandemic and the Covid-19 lockdown period influenced mood-behavioral functioning of children with ADHD.	Sleep duration showed no or low influence on internalizing and externalizing behaviors after control for age, sex, and socioeconomic status. Patients with ADHD with "no sleep problem" showed significant lower scores in internalizing and externalizing behaviors than those who "maintained" or had "onset" of different sleep problems.
Cetin et al 2020	Cross sectional	76 children with ADHD and their parents	53 boys, 23 girls	52 – Methylphenidate 24-Atomoxetine	8-12 years	To investigate the relationship between chronotype preference/sleep problems and symptom severity of children with ADHD during the COVID-19 outbreak and to assess the chronotype preference/sleep problems that may play a mediating role between the reactions to trauma and severity of ADHD symptoms.	There were significant differences in trauma symptoms and CSHQ scores between the eveningness type group and the non-eveningness type group. In mediation analyses, sleep problems were found to be the full mediating factor in the relationship between trauma symptom scores and severity of ADHD symptoms.

Levelink et al. 2021	Longitudinal	2768 mother-child pairs	1414 male children	-	Children assessed at 2, 4, 6 years and ADHD assessment between 8-10 years.	To evaluate longitudinal associations between recreational screen time and sleep in early childhood, and ADHD at age 8 to 10 years.	Longitudinally, neither screen time nor sleep were associated with ADHD. Cross-sectionally, CBCL/2-3 externalizing symptom scores increased by 0.03 with every hour television time (95% CI 0.002–0.05) and increased by 0.02 per hour of less sleep (95% CI −0.03–−0.01).
D'Agati et al.2020	Case control	Total 111 children ADHD - 36, ASD -38, TD – 37	ADHD group- 12 girls, 24 boys, ASD group – 16 girls, 22 boys, TD group – 12 girls, 24 boys	ADHD and ASD children drug naive	7-13 years	To investigate the presence of sleep problems in a sample of ADHD and ASD patients without intellectual disability. Parents completed the Children's Sleep Habits Questionnaire (CSHQ) and the Parenting Stress Index-Short Form (PSI-SF).	The ADHD group showed significantly higher scores on all the CSHQ, and the PSI-SF subscales compared to the TD group and on all PSI-F subscales compared to the ASD group.
Yin et al. 2022	Case control	Total 100 children, ADHD – 66 ADHD + sleep disorder - 47	70 boys, 30 girls	Medication naive	4-16 years	To explore the correlation between sleep disorders and ADHD in children.	Sleep disorder group had higher ADHD measure score than non-sleep disorder group ($P < 0.05$). Children with sleep disorders showed higher ADHD symptom values (inattention, hyperactivity/impulsivity, and oppositional defiance) than children without sleep disorders ($P < 0.01$). Moderate correlation between SDSC scores and SNAP-IV scores ($r = 0.486$, $P < 0.05$). Effect of Arousal disorder and Sleep–Wake Transition Disorder scores on SNAP-IV (ADHD measure) scores was found ($P < 0.05$).

Mimouni-Block et al. 20	Case control	ADHD - 25, ADHD + typical sensory profile - 13, Control group - 38	42 boys, 34 girls	20 ADHD children on stimulant medication	8-11 years	To evaluate whether SMD (sensory modulation difficulties) are associated with sleep difficulties in children with ADHD	Sleep difficulties were detected in 86.4% of children with ADHD + atypical SSPs, as compared to 30.8% of children with ADHD + typical SSPs, and 16.7% of controls. Children with ADHD and atypical SSPs had significantly increased odds for sleep difficulties as compared to controls (OR = 32.4; 95% CI 4.0–260.1, p = 0.001), while children with ADHD and typical SSPs were indistinguishable from controls.

Summary of studies focussing on macro-structural sleep properties among ADHD children

Authors/publication year	**Study Design**	**Participant characteristics**				**Objective**	**Summary of main results**
		Sample size and diagnosis	**Gender (male%/female %)**	**Medication use**	**Age**		**Interventions/Comparisons /Outcomes**
Ziegler et al. 2021	Case control	Total 57 ADHD - 24 Non-ADHD - 33	42 boys, 15 girls	In ADHD group, Stimulants - 19, Atomoxetine - 1	6-12 years	To examine sleep variables in children with ADHD, addressing their intra-individual variability (IIV) and considering potential precursor symptoms as well as the chronotype.	Children with ADHD showed longer sleep onset latency (SOL), higher IIV in SOL, more movements during sleep, lower sleep efficiency, and a slightly larger sleep deficit on school days compared with free days. No group differences were observed for chronotype or sleep onset time.

Summary of studies focussing on micro-structural sleep properties among ADHD children							
Authors/publication year	**Study Design**	**Participant characteristics**				**Objective**	**Summary of main results**
		Sample size and diagnosis	**Gender (male%/female %)**	**Medication use**	**Age**		**Interventions/Comparisons /Outcomes**
Fasano et al. 2022	Cross sectional	N = 70 Diagnosed with ADHD-H and ADHD-C	58 boys, 12 girls	-	3-17 years	To investigate whether slope of the Slow Waves (SWs), was a potential predictive parameter for psychiatric comorbidities and neuropsychological dimensions in ADHD.	Correlations of Maximum Downward Slope (MDS) of SWs with multiple anxiety disorders, CBCL scores, autistic traits and slower processing speed score on WISC-IV.
Özbudak et al. 2022	Case control	ADHD = 35 Healthy children = 32	38 boys, 29 girls	Medication naive	7- 17 years	To look for a new, simple, inexpensive, and an easily detectable electrographic marker in the diagnosis of ADHD by using electroencephalography (EEG).	Slow sleep spindle's amplitude, duration, density and activity are significantly higher in ADHD group (most significant in ADHD-I) than the HC group ($p < 0,05$). Sleep spindle's features are not statistically significant between in ADHD subgroups.
Furrer et al. 2020	Case control	ADHD = 15, Healthy control group = 15	26 boys, 4 girls	7 ADHD children on stimulants, 7 stimulant naïve, 1 took stimulants till	9-15 years	To examine relationship between learning and SWA in children with ADHD.	Control group showed expected right-parietal increase in sleep SWA after visuomotor learning.

				2 years before.			
Ueda et al 2020	Case control	ADHD = 31 Typically developing children (TDC) = 17	31 boys, 17 girls	No participants took any medications.	6-15 years	This study focussed on differences in EEG functional connectivity during NREM stage 1 between children with ADHD and controls.	central-to-posterior gamma phase lag index (PLI) was lower in children with ADHD than that in TDC. Higher hyperactivity scores and low reaction times on CPT linked with low motor and occipital pairs of gamma PLIs.
Lewis et al. 2022	Cross sectional	Parent offspring ADHD trios = 328	101 females	ADHD medication = 214, Sleep medication = 76	5-18 years	To test whether, in children with ADHD, polygenic liability for sleep phenotypes is over- or under-transmitted from parents,	Children's insomnia and chronotype polygenic liability scores (PGS) did not differ from mid-parent average PGS but long sleep duration PGS were significantly over-transmitted to children with ADHD.
McCabe et al.2023	Case control	367 total children. ADHD – 112, TD - 255	ADHD group – 18 girls TD group – 117 girls	ADHD children not on any psychotropic medication	7-12 years	To replicate previously reported EEG characteristics between TD children and two subtypes of ADHD using a frontal, single-channel, dry-sensor portable EEG device. Participants had frontal EEG recorded during eyes-closed resting, eyes-open resting, and focus tasks.	Frontal delta and theta power significantly increased in the ADHD-C compared to ADHD-I and TD groups.
Castelnovo et al. 2022	Case control	ADHD - 30 TD - 23	ADHD group- 21 boys, 9 girls TD group – 13 boys, 10 girls	Drug naïve ADHD children	8-14 years	To investigate sleep power topography in all traditional frequency bands, in all sleep stages and	Compared to TD subjects, patients with ADHD consistently displayed a widespread increase in low-frequency activity (between 3 and 10 Hz) during NREM sleep, but not

						across sleep cycles using high-density EEG.	during REM sleep and wake before sleep onset.
Ruiz0Herrera et al. 2021	Cross sectional	74 children diagnosed with ADHD	58 girls, 16 girls	48 children on ADHD medication	7-11 years	To investigate whether sleep spindle activity, which has been associated with brain maturation.	Children with ADHD showed a higher number and density of slow compared to fast spindles which were more frequent in frontal area. No differences were observed among ADHD presentations for any spindle characteristics. Spindle frequency and density increased with age, but not IQ.

Summary of studies focussing on circadian rhythm markers among ADHD children							
Authors/publication year	**Study Design**	**Participant characteristics**				**Objective**	**Summary of main results**
		Sample size and diagnosis	**Gender (male%/female %)**	**Medication use**	**Age**		**Interventions/Comparisons /Outcomes**
Zeron – Rugerio et al. 2021	Case control	ADHD = 60 Control group = 60	68 boys, 52 girls	Medication naive	6-16 years	To study circadian patterns of motor activity in subjects with ADHD and to investigate relations between alterations in circadian patterns, the ADHD subtype, sleep disturbances and body mass index (BMI).	ADHD group showed trend towards eveningness, greater sleep disturbances than controls. ADHD-C had higher mean values of motor activity and delay in bedtime. For ADHD-I, increased fragmentation of circadian pattern was associated with inattention symptoms, and had increase in BMI of 2.52 kg/m^2 in comparison with controls.
Sanabra et al .2020	Cross sectional	From a total of 60 children diagnosed with ADHD, 30 started stimulant drug treatment	34 boys, 26 girls	Medication naive	6-16 years	To analyse activity patterns in children with ADHD during a 24-hour period for seven days, before and after taking stimulant drug treatment (methylphenidate).	There are significant differences before and after carrying out the treatment, with higher levels of activity in patients with ADHD before starting treatment and a decrease in this activity after drug treatment.

Summary of studies focussing on consequences of sleep functioning in children with ADHD							
Authors/publication year	**Study Design**	**Participant characteristics**				**Objective**	**Summary of main results**
		Sample size and diagnosis	**Gender (male%/female %)**	**Medication use**	**Age**		**Interventions/Comparisons /Outcomes**
Munz et al 2022	Experimental Case control	N = 58, ADHD = 28 Typically functioning children = 30	58 boys	ADHD medication refrained for 48 hours prior to study	8-12	To investigate sleep associated odor memory consolidation in ADHD and typically functioning children after a night of sleep Vs wake.	Odor memory consolidation was superior in the ADHD sleep group compared to the TDC sleep and the ADHD wake groups.
Li et al. 2022	Case control	ADHD with Insomnia = 36, ADHD without insomnia = 27, healthy control group = 21	58 boys 26 girls	Full study not released yet.	6-12 years	To examine association of insomnia symptoms with daytime behavior and cognitive functioning in children with ADHD.	ADHD + insomnia group had the highest scores on ADHD measures, followed by children with ADHD without insomnia and healthy controls (all $P < .05$). ADHD + insomnia group showed poorer performance on the CPT and Letter-digit than other groups.
Dharweesh et al. 2021	Case control	ADHD = 42 Healthy children = 42	48 boys, 36 girls	Medication naive	6-12 years	To compare the subjective and objective sleep parameters among children with and without ADHD.	ADHD group had more CSHQ assessed subjective sleep problems, PSG measured decrease in total sleep time, sleep efficiency, spending more time in wake and N1 sleep stages. lower REM sleep duration. For this group, REM sleep duration

							predicted QoL and school function impairment.
Lambek et al. 2021	Cross sectional	59 ADHD children	41 boys, 18 girls	Medication naive	6-14 years	To examine sleep problems and neuropsychological deficits using parent report (CSHQ), PSG and multiple sleep latency test along with executive function objective test and ratings.	The correlations between sleep and neuropsychological outcomes were generally modest, but some sleep parameters (primarily sleep stages and sleep latencies) were associated with objectively and subjectively measured executive function and delay aversion.
Mann et al. 2020	Case control	ADHD = 73 Control group = 73	94 boys, 52 girls	From ADHD group, 19 on medications, 13- stimulants, 2- atomoxetine, 4 – fluoxetine, risperidone – 3 and clonidine - 3	10.5- 13.5 years	To use Bayesian analyses to examine the relationship between ADHD symptoms, sleep problems, and inhibition.	ADHD symptoms are associated with sleep problems and reaction time variability, however, sleep problems accounted for more variance in inhibition performance than both hyperactive and inattentive symptoms.
Davidson et al. 2022	Case control	ADHD – 18 TD - 18	28 boys, 8 girls	ADHD children were medication naive	6-11 years	To determine impact of sleep restriction on daytime functioning. Children participated in two sleep conditions: Restricted condition required a 1 h reduction of time in bed for one week, and the Controlled Typical condition was based on	Many daytime functions were not affected by this very mild sleep restriction, however, both groups showed significant changes in performance on an objective attention task and on a parent-rated emotional lability measure after six nights of minimal reductions in TST. There were no significant differences between groups.

						participant's average baseline sleep. At the end of each condition, participants has PSG recording and daytime functioning assessments.	
Cremone-Ciara et al. 2020	Within subject sleep extension intervention	ADHD – 11 Non-ADHD - 15	ADHD group – 2 girls 9 boys, Non-ADHD group – 5 girls, 10 boys	6 children with ADHD on medication during study	8-12 years	To determine whether sleep extension improves inhibitory control, a primary cognitive deficit in ADHD. Sleep was assessed with actigraphy and polysomnography. Inhibitory control was assessed with a Go/No-Go task.	For children without ADHD, there was a significant main effect of time, such that morning inhibitory control was 10% greater than evening inhibitory control. For children with ADHD, morning inhibitory control did not differ from evening inhibitory control, sleep extension improved inhibitory control by 13% overall.
Ruiz-Herrera et al. 2021	Cross sectional	91 ADHD children (29 - ADHD-I, 32 - ADHD-H, 31- ADHD-C)	73 boys, 18 girls	Children abstained from ADHD medication 36 hours prior to study.	7-11 years	To examine the influence of parent-reported and polysomnography (PSG)-measured sleep patterns on the academic and cognitive performance of children with ADHD.	Academic performance was predicted by the following sleep variables: Sleep time, time in bed, night awakenings, and daytime sleepiness. The best predictors of cognitive performance in children with ADHD were rapid eye movement latency, light sleep, periodic limb movements index (PLMs), awakenings, and daytime sleepiness.
Kim et al. 2022	Case control	Total 341 children. ADHD - 155 Control - 186	227 boys, 113 girls	-	6-10 years	To investigate the associations between sleep-disordered breathing (SDB) and behavioral and cognitive functions	In the ADHD group, the high-risk SDB children showed significantly higher scores than the low-risk SDB group in externalizing problems ($F = 4.22$; $P = 0.042$), including hyperactivity ($F = 4.65$; $P = 0.033$) and

						in children with and without ADHD	attention problems (F = 8.19; *P* = 0.005), but not internalizing problems. Meanwhile, in the control group, the high-risk SDB children showed significantly higher scores than the low-risk SDB group in internalizing problems (F = 9.89; *P* = 0.002), depression (F = 9.45; *P* = 0.002), and somatization (F = 7.83; *P* = 0.006), as well as in externalizing problems (F = 7.72; *P* = 0.006), including hyperactivity (F = 6.23; *P* = 0.013), aggression (F = 5.00; *P* = 0.027), and conduct problems (F = 6.79; *P* = 0.010). None of the attention subscale scores showed differences between the high- and low-risk SDB groups in either the ADHD or control group.
Villalba-Heredia et al. 2021	Case control	Total 75 children. ADHD – 47, Control group - 28	48 boys, 27 girls	44 ADHD children on medication	6-12 years	To analyze the relationship between sleep and academic performance, comparing children with ADHD and a control group without ADHD.	ADHD influenced the amount of sleep during weekends, the time getting up at the weekends, weekday sleep efficiency, as well as academic performance.
Munz et al. 2022	Case control	Total 24 children ADHD – 12 TDC - 12	100% male	7 ADHD children where on MPH, what was retrained 48 hours before study	9-11 years	To examine the effect of exercise and rest condition on declarative memory. Declarative memory was encoded before exercise or rest and retrieved before and	Exercise in TDC but rest in ADHD lead to a transient destabilization of declarative memory, while there were no more differences after a night of sleep. Rapid eye movement (REM) sleep latency was prolonged after exercise in both groups.

						after a night of sleep.	
Holingue et al. 2021	Case control	Total 735 children (323 TD, 177 ASD, 235 ADHD)	550 boys, 185 girls	Clinical groups asked to retrain from medication 48 hours prior to study	8-12 years	To investigate associations of parent-reported sleep measures from the CSHQ with parent-reported measures of Eexecutive functions and performance-based processing speed with each clinical population.	Higher CSHQ scores were associated with poorer EF on all BRIEF scales, across all child groups, Co-occurring symptoms of inattention and hyperactivity/impulsivity further accounted for the associations between sleep and EF. Poor sleep was not significantly associated with processing speed.
Takahasi et al. 2022	Cross sectional	835 children	408 boys, 427 girls	-	8-9 years	To examine whether sleep problems and polygenic risk scores for attention-deficit/hyperactivity disorder are associated with hyperactivity/inattention symptoms in children	Delayed sleep onset was associated with hyperactivity (coefficient [SE], 11.26 [2.87]; $P < .001$), inattention (coefficient [SE], 9.16 [2.91]; $P = .002$), and total symptoms (coefficient [SE], 9.83 [3.17]; $P = .002$). Delayed sleep onset was associated with hyperactivity (coefficient [SE], 18.57 [4.37]; $P < .001$), inattention (coefficient [SE], 16.92 [4.84]; $P < .001$), and total symptoms (coefficient [SE], 21.19 [4.77]; $P < .001$) only in the group with a low genetic risk for ADHD.
Mancini et al. 2020	Cross sectional	72 children with ADHD	-	-	6-14 years	To examine whether sleep difficulties and motor coordination problems are	Motor coordination, but not sleep difficulties, predicted additional variance in peer problems after controlling for inattention, hyperactivity/impulsivity,

						additional predictors of peer problems in an ADHD population.	internalizing problems, oppositionality, and conduct problems.

Summary of studies focusing on non-pharmacological interventions and their impact on sleep and overall functioning among children with ADHD							
Authors/publication year	**Study Design**	**Participant characteristics**				**Objective**	**Summary of main results**
		Sample size and diagnosis	**Gender (male%/female %)**	**Medication use**	**Age**		**Interventions/Comparisons /Outcomes**
Fried et al. 2022	Pilot intervention study,	N = 18, children diagnosed with ADHD	14 boys, 4 girls	-	6-12 years	To investigate the usefulness of the pediatric version of Headspace (4-week pilot study), a digital mindfulness program, for reducing stress and sleep problems.	Parent completed Becks Anxiety Inventory and CSHQ at start and end of intervention to report significant reduction in comorbid anxiety and sleep problems.
Prehn-Kristensen et al. 2020	Double blind placebo controlled study	Total = 29, ADHD = 14	All participants males	-	8-12 years	The present study aimed at enhancing slow oscillations (SO) activity using closed-looped acoustic stimulation during slow-wave sleep in children with ADHD.	The stimulation successfully induced SO activity during sleep in children with and without ADHD. After stimulation, only healthy children performed better on high-rewarded memory items., children with ADHD benefitted from stimulation with respect to procedural as well as working memory task performance.

Zaccari et al. 2022	RCT	32 children with ADHD MOM training = 16, Active control condition = 16	23 boys, 9 girls	Non medicated children	7-11 years	To test the efficacy of Mindfulness-Oriented Meditation (MOM) training)on sleep quality and behavioral problems in children with ADHD. Children randomly assigned to MOM group and Active control group (emotional awareness and recognition program.)	Objective and subjective measures of sleep quality and behavioral measures, collected before and after the programs, showed positive effects of MOM group on sleep and behavioral measures.
Sciberras et al. 2022	RCT	32 paediatricians, 27 psychologists were trained to provide 183 families behavioural sleep interventions	Children- 85 boys	Stimulant - 95 Melatonin - 41	Child – 5-12 years, Clinicians – 25-65 years,	To explore clinician and parent views of a brief training program in managing sleep problems in children with ADHD.	Clinicians' feelings of competency and confidence in managing sleep difficulties increased from pre-to post-training, while perceptions of barriers decreased. Increased parent-reported use of sleep strategies was associated with improved sleep at 3 and 6 months post-randomisation.
Sciberras et al 2020	RCT	244 children with ADHD Intervention group – 114 (completed 94) Control group - 122 (completed 89)	156 boys, 27 girls	ADHD medication - 160	5-13 years	To determine whether a behavioural sleep intervention for children with ADHD leads to sustained benefits; and (2) examine the factors associated with treatment response. The two-session intervention covered sleep hygiene and standardised behavioural strategies. The control group	Intervention children were less likely to have a moderate/severe sleep problem by parent report at 12 months compared to usual care children (28.4% v. 46.5%, $p = 0.03$). Children in the intervention group fared better than the usual care group in terms of parent-reported ADHD symptoms (Cohen's d: -0.3, $p < 0.001$), quality of life (d: 0.4, $p < 0.001$), daily functioning (d: -0.5, $p < 0.001$), and behaviour (d: -0.3, $p = 0.005$) 12 months later.

						received usual care. Post intervention outcomes at 12 months.	
Mehri et al. 2020	Parallel two-armed RCT	Total – 56, Intervention group – 28, control group-28	-	-	6-12 years	To examine the effect of behavioral parental training (BPT) on sleep problems in children diagnosed with ADHD	Intervention group experienced a significant improvement in total sleep scores two months after the intervention compared to the control group ($p = 0.03$). Also, the findings showed a significant decline in total sleep problems in the intervention group compared to the control group over time ($p = 0.01$).
Liang et al. 2021	Cross sectional	56 children diagnosed with ADHD.	84% boys	-	6-12 years	To study the mediating role of sleep in the relationship between physical activity and executive function in children with ADHD. Four sleep parameters, including sleep latency (SL), sleep efficiency, total sleep time, and wake after sleep onset were recorded from the actigraph. Three core executive functions, inhibitory control; working memory (WM); and cognitive flexibility (CF), were assessed from computer-based tasks.	MVPA was negatively associated with SL (−0.169; 95%CI [−0.244, −0.112]). WM (total scores) was positively related to MVPA (0.028, 95%CI [0.008, 0.048]), but negatively related to SL (−0.105, 95%CI [−0.167, −0.030]). CF (part B errors) was negatively associated with MVPA (−0.031, 95%CI [−0.055, −0.005]) and positively correlated with SL (0.184, 95%CI [0.092, −0.260]). The indirect effect of SL was found for MVPA and WM (0.018, 95%CI [0.015, 0.034]), supporting the indirect partial mediation. Similarly, the indirect effect of SL was found between MVPA and CF (−0.031, 95%CI [−0.060, −0.012]), supporting the indirect partial mediation.

Bolic Baric et al. 2021	Intervention study	Total 85, Children- 48 (out of which, ADHD – 29, ASD – 2, ASD+ADHD – 11, ADHD + comorbidity – 5, ASD+ comorbidity - 1)	In child group- 66.7% boys	-	Child group = 7-17 years	To investigate whether the use of a weighted blanket has a positive impact on sleep and everyday activities in individuals with ADHD and/or ASD.	Weighted blankets showed positive impact on falling asleep, sleeping the whole night, and relaxing during the day, and they were used frequently by children and adults with ADHD and/or ASD
Larsson et al. 2021	Qualitative study	24 parents	Parent- 18 mothers, 6 fathers Child- 12 boys, 12 girls	Drug naive	6-15 years	To explore parents' experiences of weighted blankets (16 weeks) for children with ADHD and sleep problems, and the impact on their children's sleep.	Parents reported that children sleeping with weighted blankets: (1) achieved satisfactory sleep, including improved sleep onset latency, sleep continuity, and sleep routines; (2) achieved overall well-being, including improved relaxation and reduced anxiety; and (3) mastered everyday life, including improved balance in life, family function, and participation in school and leisure activities.
Sahin et al 2021	Cross sectional	85 children with ADHD	55 boys, 30 girls	Drug naive	7-12 years	To examine sleep and social cognition in children with ADHD.	Hierarchical multiple regression analyses were performed to determine predictive factors of the Reading the Mind in the Eyes Test (RMET) and Faux Pas Recognition Test (FPRT). There was no significant relationship between CSHQ and social cognition RMET score. Lower executive function score on Stroop test part V was associated with higher social cognition FPRT score ($p = 0.002$) and

							higher social cognition RMET score ($p < 0.001$). Sleep disturbance and EF are both associated with social cognitive impairment, sleep particularly with the cognitive component.

Summary of studies focusing on pharmacotherapy and its effect on sleep among ADHD children							
Authors/publication year	**Study Design**	**Participant characteristics**				**Objective**	**Summary of main results**
		Sample size and diagnosis	**Gender (male%/female %)**	**Medication use**	**Age**		**Interventions/Comparisons /Outcomes**
Cataldo et al .2022	RCT	Children – 148 diagnosed with ADHD	PRC – 28 girls, 47 boys, Placebo – 24 girls, 49 boys.	Prior stimulant use- PRC – 43 Placebo - 52	6-12 years	To compare the effect of a once-daily extended-release methylphenidate formulation (PRC-063) versus placebo on sleep, measured via daily electronic diary in children and adults.	When compared with the diaries of placebo patients, the sleep diaries in pediatric patients showed no statistical difference in total sleep time, efficiency, or latency.
Corkum et al. 2020	RCT, crossover medication trial with 2 conditons. 2 weeks placebo, 2 weeks MPH treatment.	26 children with ADHD	23 boys, 3 girls	Medication naive	Means age – 8 years	To investigate the impact of extended-release MPH on sleep using both actigraphy and polysomnography (PSG).	Total sleep time was reduced by 30 minutes and sleep onset latency was increased by 30 minutes in the MPH condition compared to the placebo condition ($p<0.001$). No differences found in sleep efficiency. No differences found for the same variables assessed by PSG; significant increase in the relative percentage of stage N3 sleep by 3.2% during MPH treatment ($p<0.05$).

Solleveld et al. 2020	Double blind 16 week placebo controlled RCT	25 children diagnosed with ADHD	100% boys	Medication naive	10-12 years	To assess effects of prolonged MPH treatment on sleep in a 16-weeks clinical trial with immediate-release MPH.	A significant time-by-treatment interaction effect ($p = 0.007$) on sleep efficiency was found. Post-hoc analyses demonstrated that the two groups did not differ from each other ($p = 0.94$) during treatment (week 8), but that sleep efficiency was significantly improved in the MPH ($p = 0.005$), but not placebo group ($p = 0.87$) 1 week after trial end.
Davidson et al. 2021	Cross sectional	50 children diagnosed with ADHD	-	Medication naive	-	To examine whether pre-treatment sleep can predict responses to treatment and the emergence of side effects.	Hierarchical regression analysis showed that parent-reported shorter sleep duration before medication treatment significantly predicted better response to treatment, independent of pretreatment ADHD symptoms.
Yektas et al. 2020	Cross sectional	62 children diagnosed with ADHD. (ADHD I – 28, ADHD- H – 8, ADHD -C- 26), MPH – 50, ATX - 12	38 boys, 24 girls	Medication naive	MHP group-mean 8.1 years ATX group – mean 8.1	To evaluate the baseline sleep habits of children with ADHD and the effects of treatment with methylphenidate (MPH) and atomoxetine (ATX) on sleep parameters.	Sleep problems at baseline was 93.5 %. At the endpoint, 83.9 % of the sample still displayed clinically significant sleep problems. Both MPH and ATX reduced symptom severity of ADHD in all domains and also reduced total CSHQ scores with similar effect sizes. (0.7 for MPH vs. 0.8 for ATX).

Impressions from the Literature Search Update:

Within the articles assessing sleep and other areas of functioning primarily through subjective reports, a majority of studies have explored sleep and comorbidities in the child through cross sectional or case control or longitudinal designs (for example, Bruni et al. 2021, Gosling et al. 2023, Melegari et al. 2023, Levelink et al. 2021). However, the publication a qualitative study exploring sleep in ADHD (Harris et al. 2022) and articles exploring the role of trauma (Cetin et al 2020) and sensory modulation (Momouni- Bloch et al 2020) in sleep and childhood ADHD marked new and emerging directions. A number of articles surfaced which explored the microstructural sleep properties through objective measures rather than the macrostructural properties. Investigations on slow wave activity and sleep staging dominated this section (for example, Fasano et al. 2022, Furrer et al. 2020, Ueda et al. 2020). For the few studies exploring circadian rhythms in this population, a trend towards eveningness was observed in the ADHD group and ADHD-I was associated with greater fragmentation in circadian patterns of motor activity.

Among studies examining the consequences of sleep in ADHD, articles mostly explored neuropsychological, behavioural, and academic performance outcomes (for example, Munz et al. 2022, Lambek et al. 2021, Ruiz-Herrera et al. 2021, Kim et al. 2022). An interesting mix of articles exploring non-pharmacological intervention for sleep and ADHD symptoms were reported, with the additions of meditation and mindfulness-based techniques (Fried et al. 2022, Zaccari et al. 2022), and interest in examining the effect of weighted blankets (Bolic-Baric et al. 2021, Larsson et al. 2021). However, behavioural interventions (Sciberras et al. 2022, Sciberras et al. 2020), parent training (Mehri et al. 2020) and physical activity (Liang et al. 2021) were also explored. Finally for studies focussing on pharmacotherapy and its effect on sleep, exploration of methylphenidate dominated the cluster (for example, Cataldo et al.

2022, Corkum et al. 2020). Therefore, while prominent trends in research have continued since we wrote our systematic review, new additions mostly of possible clinical utility have surfaced.

Chapter 3:

“Tell me more about your child’s sleep”: A qualitative investigation of sleep problems in children with ADHD.

This chapter has been submitted to the journal: Behavioural Sleep Medicine

Status- Undergoing peer review.

Abstract

This study qualitatively investigated the nature of sleep problems in children with Attention Deficit Hyperactivity Disorder (ADHD) and their impacts on the children, their caregivers and their households. Semi-structured interviews were conducted with twenty-six parents of pre-adolescent children (aged 6-12 years) with a diagnosis of ADHD. Collected information from the interview transcripts were subjected to thematic analysis. Three themes were generated from the data: Children's sleep difficulties (sub-themes of difficulty initiating sleep, emotional distress affecting sleep and waking early despite late sleep onset); Impacts of children's sleep problems (sub-themes of behavioural and emotional consequences of sleep problems, influence of children's sleep on parents' sleep/evening schedule and sleep problems as a motivation for ADHD assessment); and Improving children's sleep (sub-themes of bedtime routine, improving children's emotional state to help sleep, bedroom features, and medication effects on children's sleep). In this study parents reported that sleep problems are significant disruptors for the children, parents themselves and for the wider household. Parents also reported utilising a variety of behavioural and sleep hygiene approaches to help their children to sleep.

3.1 Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterised by inattention, hyperactivity, and impulsivity, and is associated with social, occupational, and functional impairments (DSM, 2013). ADHD is consistently associated with sleep disturbances; core symptoms of ADHD may negatively impact sleep, whilst poor quality sleep may worsen ADHD symptoms (Raman & Coogan, 2019; Lam & Lam, 2021). Further, both stimulant and non-stimulant ADHD medication may contribute to sleep problems in ADHD (Clavena and Bonati, 2017). The nature, and clinical and psychosocial significance, of sleep problems in ADHD are not precisely defined, but are reported to include decreased parental-rated sleep quality, longer sleep onset latencies, greater bedtime resistance and more night-time awakening and such sleep problems in ADHD are associated with externalizing and internalizing symptoms, sluggish cognitive tempo and are predictors of subsequent ADHD trajectories (reviewed in Bondopadhyay et al., 2022). It is not clear whether sleep disturbance in ADHD has specific features or is similar to sleep problems that occur trans-diagnostically in young people (Arns et al, 2021). In order to address this important issue, more granular and contextual understanding of sleep disturbances is required in ADHD, it's co-occurrences and its differential diagnoses.

ADHD and sleep disturbances in children may also impact on parental sleep and mental health (Buxton et al, 2015). Such decrease in parental wellbeing may in turn decrease parents' ability to implement effective sleep management strategies for their children and adversely impact other parenting behaviours (Bordeleau et al, 2012; Martin, 2019). Sleep problems in ADHD associate with poorer parental sleep quality (Matsouka et al 2014), with maternal anxiety and depression (Martin et al, 2021) and that children's sleep impact family relationships (Harpin, 2005), with parents of children with ADHD expressing greater role dissatisfaction (Podolski and Nigg, 2001). Higher levels of children's pre-sleep arousal and

anxiety predicts poorer parental sleep quality (Bar et al, 2016), and an intervention for sleep problems in children with ADHD decreased parental anxiety (Sciberras et al, 2011).

Most studies of sleep in ADHD rely on subjective parental report through instruments; whilst these approaches are well-established in sleep medicine, parental ratings of children's sleep may be biased by specific symptomatic features and comorbidities, as well by family psychosocial circumstance (Sciberras et al., 2016, 2017). Further, whilst quantitative approaches to sleep in children with ADHD are undoubtedly of value, they lack the granularity and contextual richness required to gain nuanced understanding of the experiences of both children and caregivers of sleep problems in ADHD. To address such issues, qualitative approaches will be of utility in developing holistic insights into sleep in ADHD and identifying unmet clinical needs, although there are currently few published studies using such approaches (Larsson et al, 2021; Harris et al, 2022). In the current study we investigated sleep in children with ADHD through semi-structured interviews with their parents and thematic analysis of transcripts to gain new contextualized insights regarding the children's sleep problems and their impacts, and parents' perceptions and attitudes towards their children's sleep. The overall aim was to deepen understanding of sleep in paediatric ADHD, its family-wide impacts and to explore areas of unmet need.

3.2 Methods

26 parents of children (6-12 years old; mean age 9.8 years) were purposively sampled from the membership of ADHD Ireland (a non-profit charity organization in Ireland; N=16) and the ADMiRE ADHD service at Linn Dara Child and Adolescent Mental Health Services, Dublin (N=10) according to the inclusion criteria of being a parent of a child aged between 5 and 12 years old with a formal diagnosis of ADHD. The ADHD status of the children was as reported by the parents and was not confirmed with clinical interview. Information Power model components were used to inform sample size (Malterud et al., 2016). Considering the elements of the study's aim, the sample specificity, the status of the established theory in this field and quality of dialogue (the extensiveness of the information that is aimed to be elicited in the interview), we inferred a smaller sample size, however when considering the analysis strategy which will include cross analysis of the interview results (through identification of code relations and its frequency across the interviews), we acknowledged that the sample size cannot be very narrow and must have a substantial number of individuals for cross coding. Keeping the above points in mind we agreed on recruiting 26 parents for the qualitative interview process. Upon informed consent, demographic information was gathered (children's age, gender, medication use, number of siblings, known co-occurring conditions for the child, parent's gender), and a semi structured on-line interview was conducted by UB with the parents alone. The study approved by the Maynooth University Research Ethics Committee and the Research Ethics Committee of Linn Dara Child and Adolescent Mental Health Services, Dublin.

A set of interview questions was constructed based on our recent systematic review of sleep in paediatric ADHD (Bondopadhyay et al 2021; Table 1). Interviews were audio recorded for transcription and analysis, with all transcribed data irreversibly anonymised. Reflexive Thematic Analysis (TA) was used to generate themes and sub-themes from the interview data

(Braun & Clarke 2006, 2019). As TA can be used with different, or combinations of, theoretical frameworks, themes could be generated and interpreted for both parents' and children's sleep issues, and the interaction between.

Some features of deductive analytical approach were used as there was a pre-existing partial conceptual framework within which to explore features of sleep and ADHD (eg. Raman and Coogan, 2019), and reflexivity were realized through the researchers' active engagement with the data and analysis that allowed for themes to be generated and interpreted in a non-pre-defined manner. To best describe our utilized methodology, an abductive approach could be highlighted, where we took the middle ground between inductive and deductive approaches (Coffey & Atkinson, 1996; Tavory & Timmermans, 2014). Therefore , the design of the study was neither completely data driven (based on previous literature demonstrating sleep problems in childhood ADHD), nor hypothesis-driven (assumptions based on UB and AC's own reasoning of the subject matter), but aimed at presenting results yielded from parallel and equal engagement with both the empirical data (as accumulated through the interviews) and extant literature (as reviewed in the first and second chapters of this thesis) (Atkinson et al 2003; Hurley et al 2021; Rinehart, 2021; Timmermans & Tavory, 2012).

Throughout the design and implementation of the study, UB maintained a self-critical stance to identify and acknowledge her own epistemological standpoint and biases, particularly in the context of UB's professional background as a psychologist working with children with ADHD. This mental set was acknowledged as potential leading to overemphasizing children's sleep problems and their impacts. The above was discussed and acknowledged during the co-analysis process with AC, who in turn recognized his biases and perspectives from a background in quantitative studies of sleep in ADHD.

Table 3.1 *Interview questions as presented in chronological order (and the rationale behind them which was not shared with parents).*

No.	Questions
1.	Tell me more about what makes a good night's sleep for your child? (to get an account of the factors helpful for sleep)
2.	Tell me more about what makes a not so good night's sleep for your child? (to get an account of factors detrimental to sleep)
3.	How do you think your child feels when they wake up in the morning? (to get account of the child's temperament in the morning)
4.	Tell me more about your child's sleep quality? (Prompts to elaborate on sleep durationand other parameters of sleep that the participant might skip such as, snoring, limb movements during sleep, breathing difficulty and the emotional reactions the person has due to these?)
5.	Tell me about your child's sleep duration through the week (weekends and weekdays) (to get an account of the weekly sleep patterns)
6.	Speaking of bedtime routines for your child, what comes to your mind and why? (to get an account of the bedtime routines, environments and activities)
7.	Can you describe the activities your child prefers before bedtime? (to get details of the activities before bedtime)
8.	How do you feel ADHD medication might/or might not be affecting your child's sleep/wake cycles? (input about the perceived role of ADHD medication)
9.	Can you describe your child's sleep and wake patterns? (Following probes on why and how they affect their functioning) (to collect information on perceived sleep related behaviors of the child)
10.	Tell me more about your child's sleeping arrangements. (to get information about sleep environments and potential sleep enabling/restricting factors)
11.	Can you describe your child's bedroom? (Probes about lighting, bed, curtains, bedding if not mentioned already after primary question) (to yield information about child's sleep environment)
12.	How important do you think sleep is for your child and how important is it do you think it is for you? (to ascertain parent's perceived level of importance of sleep for child and themselves).

The following section illustrates the thematic analysis process in detail:

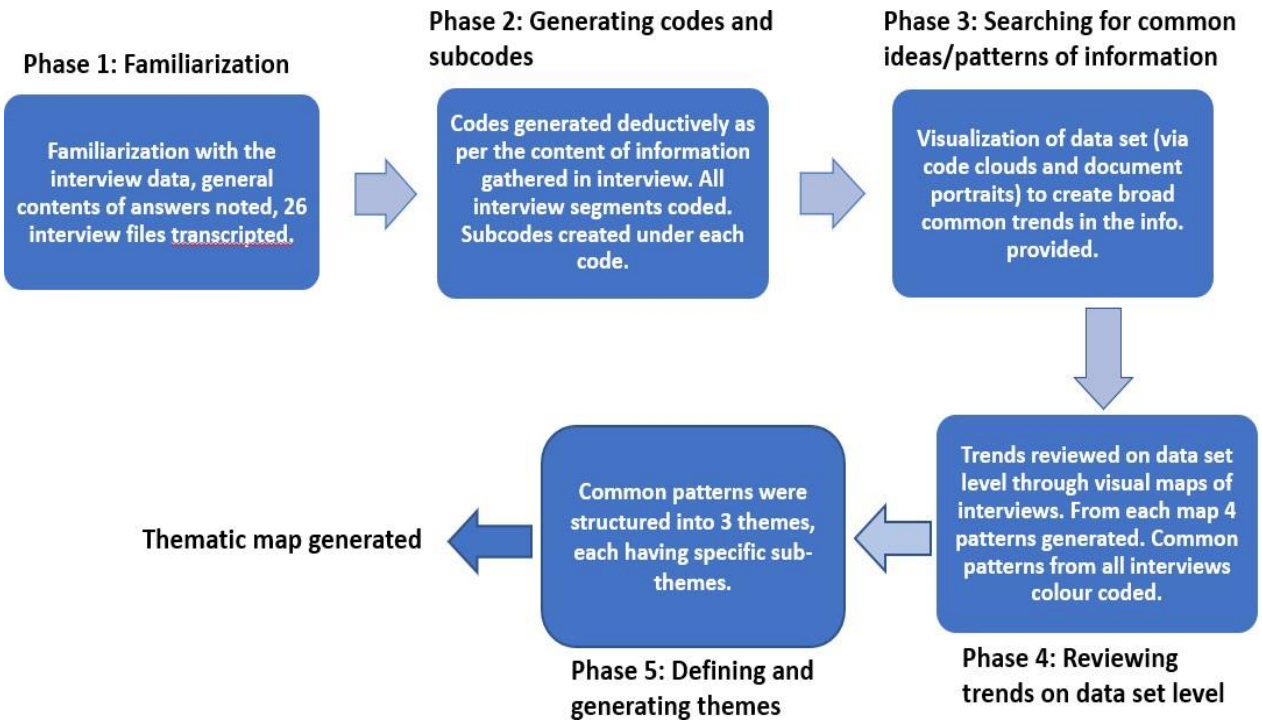


Figure 3.1. *Flowchart illustration of the Thematic Analysis process*

Note. Six phases of thematic analysis were utilised to analyse the interview data (Braun and Clarke, 2006, 2019).

Phase 1: Familiarization with the data involved listening to each interview and noting the general content of the answers. Notes made during this phase proceeded to Phase 2 of the analysis pipeline. Recorded interview was then transformed into a written format through a software assisted transcription system (Otter.ai). In the process of developing the final 26 individual transcripts for the interviews, all transcribed data were re-read and typing errors removed, thereby building on the process of familiarising with the transcripts.

Phase 2: We created a set of codes based on the answers from five areas that we explored in the interviews (presence of sleep problems, children's sleep hygiene, children's sleep timing, children's sleep environment and perceived effects of medication use and medication related information). Codes were created and entered in MAXQDA (Verbi

Software, Germany), and all relevant interview segments were coded. Careful review of the generated codes was conducted by UB and AC, and these codes are described below. Each code was represented by a particular colour on MAXQDA application. Following this process, MAXQDA was used to create a code map for the entire data set (Figure 3.2) based on the number of times two codes have been assigned to a segment together, thereby forming a visual illustration of the structure in which codes occurred in the interviews. Subcodes generated represented second-order tags assigned to enrich the entry of the primary code.

Table 3.2 *List of codes generated.*

Code	Description
Factors helping sleep	This code describes all information relating to parents' efforts to help their child sleep at night. This code includes information on sleep environments deliberately formed by parents, pre-sleep activities, pre-sleep dialogues, planned day-time activities, medication/interventions as well as parent's own behaviours to promote the children's sleep.
Night-time behaviours of the child	This code describes all information provided by parents about the child's activities after dinner/evening supper, leading up to bedtime and sleep onset. Here, information such as night-time routines and schedules, parental observed behaviour patterns and the psychological state of the child is included. This code includes two sub-codes: "Behavioural concerns at night" and "Effects on parents".
Child's bedroom details	This code describes all information provided about the child's sleeping environment, including their bed, sleeping arrangements, bedroom details, toys/items they take to bed, types of bed sheets/duvets/blankets. This code includes two sub-codes "Lighting in the bedroom" and "Distractions in the bedroom"
Sleep Quality	This code relates to information about disrupted sleep, nightmares, frequent awakenings, breathing difficulties, body movements, bed wetting or any other detail. This code includes a detailing sub code "Body movements and breathing difficulties"
Sleep duration	This code describes the children's sleep schedules, including when they generally go to bed and fall asleep, and when they wake up the in the morning, and transitions between sleep and wake. This code includes a detailing sub code "Weekend/weekday sleep duration"
After-wakening morning behaviours	This code captures all after-wakening morning behaviours of the child, including their psychomotor speed, temperament, verbal dialogues, activities they engage in and their consequences. This code contained the detailing sub code "Difficulties during morning"
Sleep/wake patterns	This code encapsulates parents' perspective on whether their child is more active/ engaging during the morning or evening time (chronotype) and perceived reasons for these preferences.
Medication	This code related to information about children's ongoing or previous medications, how it has affected their sleep and functioning; details of ADHD medications and sleep medication is included. This code includes a detailing sub code "Effects of medication on sleep"
How important is sleep	This code covers parental perceptions on how important sleep is for their child's functioning and how important is sleep for their own functioning.

	Typically parents were asked to rate the importance on a scale of 1-10 (10 being highest), however some parents have also chosen to describe the importance rather than present a numerical value.
General thoughts about child's sleep	This code covers information capturing parents' overarching thought about their child's sleep; for example, whether sleep has been an issue always, or sleep is a matter of schedules, or if sleep is not a problem in the household. This code includes a detailing sub code "Sleep's role in the diagnostic process, capturing information on how difficulties with sleep initially led to the assessment process and subsequent interventions for ADHD."

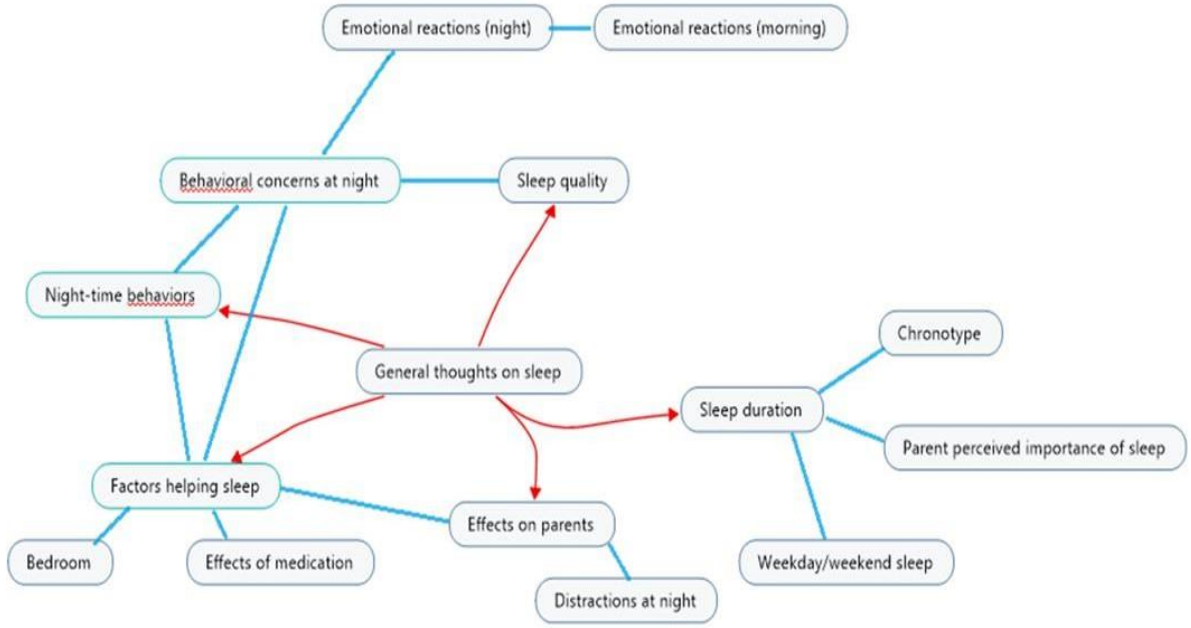


Figure 3.2 *Code map for the interview data*

Note. Code map for the interview data, derived from counts of the number of times two codes have been assigned to a segment together, allowing a visual illustration of the structure in which the codes occurred in interviews. Red connectors denote the links between General thoughts on sleep with Night time behaviour, Factors helping sleep, Effects on parents, Sleep duration and Sleep quality, which signifies the central relationship in the map, with rest of the elements being linked via blue connectors.

Phase 3: This phase involved searching for broad themes by visualising the data as a whole via MAXQDA tools of code clouds and document portraits.

Code Cloud: This tool helped visualize the most frequently assigned codes in the coded segments of the interviews. From the code cloud (Figure 3.3) it was evident that the greatest number of coded responses falls in the participant's report of factors helping sleep for their child, followed

by the parent's general thoughts on their child's sleep and the night-time behaviours (concerns) encountered for their child.

Figure 3.3 *Code Cloud from the data set*

Document Portrait: This tool helped to visualise the sequence in which the coded segments appeared in the interview and therefore brings forward the structure of the answers (Figure 3.4). This shows specific trends present in the answers, partially mirroring the structure of the interview. Nevertheless, parents presented their views on open ended questions that therefore did not restrict the conversation content to a particular topic. Document portrait colours represent that parent have usually started with either of the two themes, night-time behavioursof their children followed by behavioural concerns at night or, sleep duration/ patterns along the week followed by how this affects parent's own sleep and the behavioural concerns at night. The predominance of the above two has therefore pointed towards the common presence of behaviours at night that might be problematic and detrimental to their and their child's sleep.

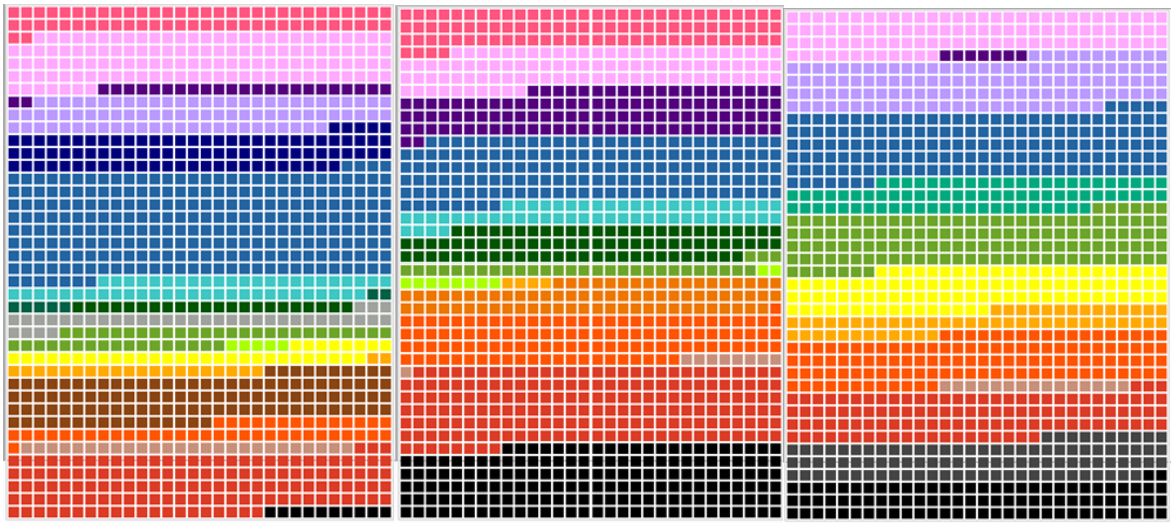


Figure 3.4 *Colour-coded document portraits for 3 interviews (each colour signifies a code)*

Phase 4: All the coded data was systematically viewed through the MAXQDA tool Visual maps, with 26 separate visual maps including all codes noted for each transcript and the data extracted for each of the codes. UB then converted the dialogues included in each code to a trend/observation format and generated four over-riding patterns for each visual map (i.e. for each interview). The example of one visual map is presented in Appendix B. These patterns are specific information trends the parent presented about their child's sleep. Common patterns from all interviews were colour coded. We generated 10 ideas that captured the core point of these patterns in our data, which were reviewed by UB and AC.

Phase 5: By structuring these ideas into relevant clusters, 3 themes were located within a thematic map:

1. Children's Sleep Difficulties.
2. Impacts of Children's Sleep Problems
3. Improving Children's Sleep

Each of the three themes had specific and clustered details associated with them which formed the basis of 10 sub-themes in total.

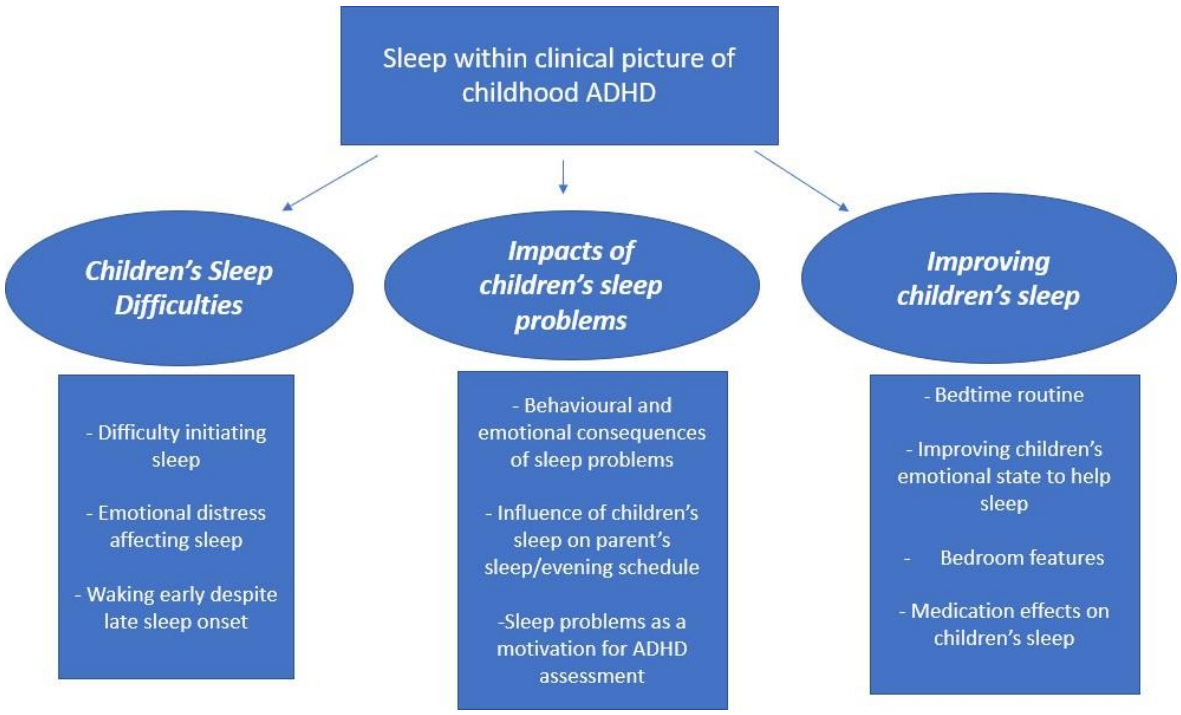


Figure 3.5 *Thematic map for the three generated themes: "Children's sleep difficulties", "Impacts of children's sleep problems" and "improving children's sleep" (and their sub-themes) under the central organising concept of "Sleep within the clinical picture of childhood ADHD".*

Phase 6: All themes were presented along with examples of interview segments in-which they were generated. Common characteristics from the 3 themes, such as the role of emotional functioning, executive dysfunction, sensory processing concerns, parent's role and effect of medication were discussed.

3.3 Results

Characteristics of the 26 children with ADHD whose caregivers were interviewed are presented in Table 3.3. In 88% of cases, the informant was the mother and 77% of the children were male. Codes were generated deductively as per the information gathered in the interviews (Table 3.2). Visualisation of the data set via code clouds, (Figure 3.3) document portraits (Figure 3.4) and visual maps for each interview's content created broad common trends. These trends were structured into three generated themes of "Children's Sleep Difficulties", "Impacts of the Children's Sleep Problems" and "Improving Children's Sleep", with between 3 and 4 sub-themes per theme (Table 3.4).

Table 3.3 *Participant demographics (N = 26)*

Measure	Frequency (%)
Child's age, Mean (Standard Deviation)	9.8 (1.77)
Male, n (%)	20 (77%)
Mother as informant, n (%)	23 (88%)
Child with siblings, n (%)	18 (69%)
Medication Use, n (%)	
Children on ADHD medication	19 (73%)
Children on ADHD medication and Melatonin	8 (30%)
Children on Melatonin only	1 (3.84%)
Known co-occurring conditions, n (%)	
Autism Spectrum Disorder	5 (19%)
Obsessive Compulsive Disorder	2 (7%)
Epilepsy	1 (3.84%)
Migraine	1 (3.84%)
History of Sleep Apnoea	2 (7%)

Table 3.4 *Generated themes and their descriptions.*

Theme	Sub-theme	Description
Children's sleep difficulties	Difficulty initiating sleep	Difficulty getting to sleep was a major pattern presented in the interviews. Parents reported their child's urge to communicate/plan/execute tasks especially during the winding down to sleep time. For example, the child might state they are hungry, need to use the toilet, complete an unfinished task. Within this theme the child's need for company during the sleep initiation time has also been noted, for example child might need mother in their room when trying to fall sleep.
	Emotional distress affecting sleep	Parents reported that emotional aspects such as fear, stress and unresolved interpersonal issues affect their child's sleep onset. Events that may have happened during the day at school, a fight with sibling, rule imposing by parents, may trigger emotional reactions that disrupt sleep initiation. Children might need reassurances, verbal outlet, support for the same by parents. Anxious thoughts about next day's events, or general anxiety about not being able to sleep was reported.
	Waking early despite late night sleep onset	This theme reflected children's tendency to wake up early regardless of difficulty falling asleep at night. This themes also described parents trying to help children stay asleep for longer, for example by using blackout blinds to reduce day light in bedroom, without reported success. Parent also delayed bedtime to later times, so the child wakes later, but to no avail, making it difficult during holidays, vacations, outings etc.

Theme	Sub-theme	Description
Impacts of the children's sleep problems	Behavioural emotional and emotional consequences of sleep problems	Accumulation of sleep deprivation, poor sleep quality and short sleep duration reported to lead to outburst after a couple of days and can manifest in the form of temper tantrums, heightened emotional reactivity or lethargy. Full-blown outburst or catching up on sleep were reported to help restore the child to previous levels of functioning. Parents acknowledgement that good sleep has significant implications for the child's behaviour, performance, and executive regulation the next day.
	Influence of children's sleep on parent's sleep/evening schedule	The timing of parents' sleep was reported to be influenced by the children's erratic sleep/wake schedules and parents having to check on the children at night. For example parents reported not being able to retire for the night and being exhausted due to the effort required arising from their child's sleep difficulties.
	Sleep problems as a motivation for ADHD assessment	This theme noted the trends where parents reported that sleep difficulties were present and significantly affected the child's daytime functioning, with these difficulties obscuring ADHD features which were later noted during further assessment. Worse sleep was noted prior to ADHD diagnosis and intervention and improved following engagement with clinical services through increased parental awareness of ADHD and increased care and support from other settings such as schools.

Theme	Sub-theme	Description
Improving children's sleep	Bedtime Routine	Parents reported taking active steps to help initiate sleep onset, such as storytelling, meditating, bargaining, negotiating, sticking to routines, and waiting in children's room. Parents reported following established routines at night, actively restricting certain activities (such as screen time)/food items (like carbonated drinks) to facilitate child's sleep. Further, parents reported that regular physical exercise such as sports, swimming and free play with friends resulted in positive influence on their children's sleep.
	Medication effects on children's sleep	Parents reported that the use of ADHD medication increased sleep onset time for the child and that Melatonin reduced sleep onset latency and was perceived as being helpful. Melatonin discontinuation was noted to result in rebound of sleep problems.
	Improving children's emotional state to help sleep	Parents reported taking steps to avoid arguments and upsetting the child before bedtime. Parents reported reassuring the child with their presence or talking about upsetting and unsettled emotions triggered during the day or evening to help induce calm and sleep for the child.
	Bedroom features	This theme related to the children's positive response to addressing sensory needs during and before sleep. These actions included engaging with specific items such as play dough, stuffed toys, a familiar blanket, providing specific tactile input, the presence of particular bedroom features such as specific duvets and bed sheets, bedroom lighting (for example use of blackout window blinds, or night lamps for optimal visual input), calming background noise for sleep inducing auditory input and optimal temperature in the bedroom.

Theme 1: Children's Sleep Difficulties

This theme related to children's difficulties in initiating and/or maintaining sleep and incorporated three sub-themes relating to specific manifestations of these issues.

Sub-theme 1: Difficulty initiating sleep (17/26 transcripts).

This sub-theme incorporated elements relating to the children's difficulties around bedtime and sleep onset, including the children's need to communicate and other non-sleep related behaviours at bedtimes, children becoming overactive and/or wanting to complete tasks/plan/execute tasks at night and children needing parent's presence in the bedroom to fall asleep.

> *''What happens is a lot of in and out of bed and up and down the stairs, 'I have something to tell you', 'I need to drink', 'I need to whatever' 'he's afraid of missing out on things.' (Male, 8 years)*
>
> *'But I've noticed before (over the years), sometimes we can't get him to sleep at night.' (Male, 10 years)*

Sub-theme 2: Emotional distress affecting sleep (8/26 transcripts).

This sub-theme related to bidirectional relationships between children's emotional distress and sleep problems at bedtime, including how children's unresolved emotions made it difficult to settle down for sleep and how emotional distress that arose from not being able to sleep was identified as a further barrier to sleep.

> '*And I think, like 90% of it is anxiety. And I think everybody has had one of those nights where you just can't go to sleep, and just stare and that is his norm.' (Male, 10 years)*

'She's like I said more agitated, more emotional. She woke during the night…she will come in and cry and scream a lot. We find that very difficult to manage.' (Female, 12 years)

Sub-theme 3: Waking early despite late sleep onset (6/26 transcripts).

This sub-theme included elements reflecting that delayed sleep onset times often did not result in later sleep offset, children's behavioural rigidity of early waking time, and how on early waking the children attempted to engage with others in the household.

'And she would wake up often at five o'clock… she would rarely sleep in even if she'd been up late the night before. So she would wake up full of energy like ready to go for the day, even if we weren't done and that was very difficult.' (Female, 12 years).

'He can wake up and he could be still tired… Trying to pacify him to stay in bed is very difficult, because he's just like… Mom and dad should be awake as well…whole house and the neighbours should be awake as well.' (Male, 8 years)

Theme 2: Impacts of Children's Sleep Problems

This theme related to the consequences of children's sleep problems, and how these impacted children's daytime function, the family context and how sleep problems contributed to initial engagement with clinical services.

Sub-theme 4: Behavioural and emotional consequences of sleep problems (9/26 transcripts).

This sub-theme included elements relating to daytime behavioural and emotional problems exacerbated following poor/short sleep, and conversely the perceived emotional and behavioural benefits of catch-up sleep.

'He wouldn't go on like, right (without sleep). No, he wouldn't like it because he wasn't functioning. He wasn't concentrating…It keeps coming back. He explodes basically screaming, shouting, kicking the walls…he starts to cry.' (Male, 7 years).

'...you know, maybe once a week, maybe once every two weeks, he might sleep on time. And that's a huge bonus…that's like, catch up sleep. You know, he obviously needed this.' (Male, 8 years).

Sub-theme 5: Influence of children's sleep on parents' sleep/evening schedule (8/26 transcripts).

This sub-theme related to impacts of children's sleep problems on their parents' sleep and evening routines, including how parents had to spend more evening time with the child at their bedtime, in turn impacting on the adult's evening schedules, and parents' own sleep being disrupted by the child's sleep problems and the need to check on the child during the night.

'... it's something that we're constantly talking about, it affects our lives every day, you know, that I'm telling her that I (mummy) haven't got any sleep…and ask her to do little things that might help me (mummy) to get a bit more sleep… I'm talking to my husband that I get no sleep.' (Female, 11 years).

'..I couldn't get to sleep, or we'd be talking about something else. And I'm lying there going, this doesn't work, I'll have to just stay in my bed, and he'll have to come in…I'll tell him… I love you…you're safe, go back…and go to sleep… that worked better.' (Male 11 years).

Sub-theme 6: Sleep problems as a motivation for ADHD assessment (6/26 transcripts).

Elements of this sub-theme pertained to the role that sleep problems played in the children's diagnosis with ADHD, how sleep difficulties led to children being prescribed medication, and increased parental awareness of the clinical features of ADHD leading to

improved functional outcomes for the children. Notably, 5 of the 6 children in question were reported as having co-morbid diagnoses (1 OCD, 2 ASD, 1 dyspraxia, 1 Migraine).

> *'So this is before we obviously hadn't really explored the ADHD diagnosis. His eyes were really heavy. He'd be moaning an awful lot at night-time…bedwetting was maybe twice a night. Was really tired… I decided maybe it was a sleep issue… so then we went down the road of being assessed by a psychiatrist, and he also had a psychology assessment…she said that he was ADHD.' (Male, 11 years*).

> *'…it has been incredibly difficult for him to fall asleep…he already had the diagnosis of Autism. But it didn't explain everything…we had gone to our GP and explained the situation with the sleep, and he put him on melatonin, he had a better quality of sleep, his ADHD symptoms in school didn't go away, but they did improve...' (Male 10 years).*

Theme 3: Improving Children's Sleep

This theme related to actions parents described taking to aid their children's sleep, including bedroom and bed features, features of the bedtime routine and how medication impacts on their children's sleep.

Sub-theme 7: Bedtime routine (20/26 transcripts).

This sub-theme comprised of elements describing active steps parents took in the run-up to bedtime, including parents using consistent evening time routines and actively restricting certain activities such as screen time and food items such as carbonated drinks. This theme also captured the perceived positive impact of children's exercise on sleep.

> *'And then just generally the routine at bedtime… And we do the same thing every night.' (Male, 10 years*).

'We don't give her carbonated drinks…she has like milk or water, or you know, she doesn't get coke or anything like that.' (Female, 12 years).

'So by about eight o'clock, he's finished supper and straight after he knows he has to brush his teeth, wash his face. And my aim for that is to be done by about half 8'. (Male, 8 years).

Sub-theme 8: Improving children's emotional state to help sleep (7/26 transcripts).

This sub-theme comprised of elements addressing how parents took steps to avoid upsetting the child before bedtime, parents reassuring children with their presence and talking about unsettled emotions to help calm the child and aid sleep onset.

'If she had a very stressful day…her sleep is mostly affected by things that have happened and overthinking…when she feels like she's had a chance to kind get those thoughts out, that makes her sleep a bit better'. (Female, 10 years).

'…it's important to not let something trigger him off. Or to try and stop it if it is starting. Because he won't sleep or won't settle easily enough.'(Male, 12 years).

Sub-theme 9: Bedroom Features (10/26 transcripts).

This sub-theme included elements relating to the use of items such as play dough, stuffed toys or a familiar blanket to aid bedtime routines, and particular bedroom features such as specific duvets/bed sheets, bedroom lighting, sounds and temperature to facilitate the children's sleep.

'Temperature is the biggest factor: it completely affects her sleep…she'll wake up exhausted because she'd be so hot.' (Female, 10 years).

'I used to play kind of relaxing music..Oh, yeah, it's smart to wind him down. I suppose just to make him relax...'. (Male, 10 years).

'She's craving deep pressure and lots of movements.' (Female, 10 years).

Sub-theme 10: Medication effects on children's sleep (12/26 transcripts)

This sub-theme related to perceived impacts of ADHD medication on sleep as well as the perceived effects of melatonin; parents reported that psychostimulants were perceived to increase sleep onset latency, whilst melatonin was perceived as being helpful.

> *'I wasn't really thinking that we will be dealing with a medication that will take him longer to unwind. And he was increased to an extra five milligrams, which didn't help taking in the afternoon, so he stayed up…I think he was just a little bit overstimulated... his eyes were dilated, and he was just kind of wide-awake running around the house.' (Male, 11 years*).

> *'So we've tried to, to see what it's like without the melatonin and he can't sleep at all. He'll stay awake until maybe half one in the morning…So, it really does have a massive benefit.' (Male, 10 years*).

3.4 Discussion

ADHD is associated with sleep disturbances during childhood, adolescence and adulthood (Bondopadhyay et al, 2021; Coogan & McGowan, 2017). However, relatively low granularity of quantitative studies has limited understanding of the nature and consequences of sleep disturbances in ADHD. Qualitative approaches are under-utilized in sleep medicine research, given their potential to reveal rich details relating to the contexts, precipitators, consequences, and management of sleep disturbances. It has previously been suggested that ADHD symptoms have a bidirectional relationship with sleep (Raman and Coogan, 2019). The current findings speak to these features through reports of parental perceptions of emotional and behavioural antecedents and consequences of poor sleep in children with ADHD, as well as the perceived benefits of improving sleep. Our findings suggest that sleep-onset difficulties are perceived as the dominant manifestation of sleep problems. Further, we identified evidence that children's sleep problems were a trigger for engagement with clinical services ultimately leading to diagnosis of ADHD, indicating the importance of assessing sleep in clinical encounters. We also note that the majority of these children had co-occurring diagnoses, highlighting the importance of such conditions in sleep problems in ADHD and the need to understand the nature of transdiagnostic sleep issues versus any diagnosis-specific sleep issues.

Emotional and Executive Dysfunction and Sleep in ADHD

Emotional distress affecting sleep was generated as a sub-theme, with children's distress resulting from difficulties falling asleep further increasing sleep onset latency. Such effects of emotional distress on sleep in ADHD has been previously reported in quantitative studies and linked to executive dysfunction (Becker et al 2016a). Children's emotional state was also associated consequences of sleep problems, with shorter sleep time perceived to be associated with behavioural/emotional outbursts and catch-up sleep leading to improved

emotional regulation. Associations of short sleep with attentional, impulsivity and behavioral problems, and their knock-on impacts on family life, echo and extend previous findings (Eyuboglu & Eyuboglu, 2018; Hiscock et al 2014), and a recent qualitative study also noted the association of poor sleep with subsequent emotional and behavioural difficulties for children with ADHD (Harris et al, 2022). Parents described taking steps to improve their child's emotional state prior to bedtime, including trying to avoid children becoming upset before bed, providing reassurance with their presence, and discussing unsettled emotions with the child. It is striking that this sub-theme was only generated in 7 of the 26 interviews, indicating a potential opportunity to enhance sleep psychoeducation for parents of children with ADHD to further emphasise the role of emotional regulation in the hours leading up to bedtime, and the potential for a virtuous circles whereby better sleep results in better emotional self-regulation for the child which then facilitates better sleep. We also found that reported rigid adherence to routines by children was associated with longer sleep onset latency and emotional problems at bedtime. Co-occurring autism-related rigid behavioural patterns may be important contributors to sleep problems in ADHD (Spruyt & Gozal, 2011), and indicate a need to better understand the role of co-occurring conditions in sleep problems in ADHD.

Previous reports using polysomnography, actigraphy and quantitative parental-report indicate that sleep onset insomnia occurs in ADHD and is linked to externalizing symptoms (Miano et al 2019; Aronen et al., 2014). As executive dysfunctions are key contributors to poor functional and psychosocial outcomes in ADHD (Brown 2017), it is important to understand the interplay between sleep and executive function. Our data suggests that executive dysfunction contributes to children's poor communication and planning around bedtime, which in turn prolongs winding down time and sleep onset latency. Erratic bedtime/evening routine may also affect other family member's sleep/ night schedules, and a desire to avoid these household disruptions may motivate parents to apply consistent bedtime routines; this sub-

theme was noted in 20 out of 26 transcripts. Previous studies have linked children's sleep problems with parental sleep and mental health (Matsuoka et al, 2014; Martin et al, 2021; Bar et al, 2016). As such, we support explicit examination of sleep as a whole-household issue for future ADHD studies. Factors that may be relevant for such investigations include family composition, bedroom arrangements (eg. single or shared), socioeconomic status, parental ADHD and mental health status and availability of social supports.

Sleep Hygiene and Bedroom Features

The importance of both executive and emotional regulation problems in ADHD suggest potential for sleep hygiene in ameliorating these impacts. Hiscock et al (2014) reported that enhanced sleep hygiene resulted in increased sleep duration and better performance on auditory working memory tasks. It is not clear if parental application of sleep hygiene practices identified in our study has been informed by psychoeducation from clinical services, by other publically-accessible sources or has been arrived at as "common sense"; future research should address this important question. We also identified that parents used bedroom features and specific items to facilitate sleep. Many children with ADHD also have sensory processing difficulties, and the use of such techniques might target these difficulties (Ghanizadeh, 2011; Hern & Hyde, 1992). Hvolby and Bilenberg (2011) reported that use of a weighted ball blanket reduces sleep onset latency in ADHD children. Larsson et al (2021) report that a trial of weighted blanket use in ADHD was qualitatively associated with better sleep, improved daytime function and reduced anxiety. A recent study found that more number of ADHD children with atypical parent reported sensory processing variabilities reported sleep problems, as compared to ADHD children without those difficulties (Mimouni-Bloch et al 2021). The current findings support adapting sleeping environments to account for sensory issues in ADHD to benefit both sleep and daytime function and may contribute to a virtuous cycle of better sleep/improved ADHD symptoms. Again, it is not obvious from the current data where

parents sourced information on the use of items such as weighted blankets and other bedroom features for their children. Bedroom features for children with ADHD will be influenced by the household status, for example in whether bedrooms are shared or single, and such considerations may constrain the extent to which parents may be able to optimize the bedroom features to aid their children's sleep.

Medication Effects on Sleep

Twelve parents mentioned use of methylphenidate formulations, and previous studies have reported methylphenidate's associations with greater sleep complaints (Becker, et al., 2016b; Childress et al., 2009), no effects (Ashkenasi 2011; Findling et al., 2009) or positive sleep outcomes (Chin et al., 2018; Morash-Conway et al., 2017). Parents reported that psychostimulant use was perceived as increasing sleep onset latency, although such impacts may be influenced by dosage, timing of dosing and drug formulation. Melatonin has uses as a somnolent and chronobiotic (Arns et al, 2021), and its use in paediatrics may be widespread (Kimland et al, 2020), although clinical guidelines for its use are not well developed (Esposito et al, 2019). An interesting facet identified was that some parents reported that sleep problems rebounded following melatonin withdrawal; it is not clear from the literature how prevalent an issue this is, and as such warrant's further investigation.

Strengths and Weaknesses

The current study has some important strengths: the application of thematic analysis reveals a richness of detail that is not available in the current literature and reveals holistic issues such as impacts of children's sleep issues on family life, parental wellbeing, and children's daytime functioning. We also identify clinically relevant facets, such as sleep disturbances as triggers for ADHD assessment that have not been previously well described in the literature. A weakness is the relatively limited clinical information that was available about

the children's ADHD, so that it is not possible to explore sleep differences between children with different subtypes or severity of ADHD. Further, the study was based on interviews with parents and as such did not directly assess children's sleep experiences. The current study only concerned pre-adolescent children; adolescence is understood as a period of profound change for young people, including sleep needs and habits (Roenneberg et al, 2004), and as such the findings may not extrapolate to adolescents. Qualitative approach may be at risk of bias in their approach to sleep research, and we acknowledge such risk in the current study although the methodology was applied systematically to reduce the risk of such bias (Mackieson, Shlonsky & Connolly, 2019). Finally, our study had a male bias (77%), perhaps reflective of a roughly two-fold greater frequency of ADHD diagnoses in boys versus girls (Hinshaw, Nguyen, O'Grady & Rosenthal, 2022).

Our study involved interviewing parents between the middle-end of 2021, a period when children's schooling systems were rapidly changing, from COVID-19 lockdown based remote learning to in-class instruction. An optimal learning environment for children with ADHD has been found to be structured settings with clear routines and need based support (Fabiano et al 2007). Whereas lockdown home learning, inherently being less structured, would further deteriorate the time management, planning, organizational skills that ADHD students are known to have concerns with (Booster et al., 2012; Langberg et al., 2013). Increased inattentiveness and hyperactivity/impulsivity in children with ADHD during the lockdown has also been reported (Melegari et al 2021; Shah et al 2021; Wendel et al 2020) Impact of the above on parents and carers on one hand, and when schools reopened, transitioning back to pre-covid schedules (making the child unlearn home based less structured learning and return to traditional classroom learning) albeit can be thought of as a difficult task for parents. Parent reports about their child's sleep wake schedule could be impacted by parent's own stress and thereby could be exaggerated. This could be perceived as a potential limitation of this study.

Conclusion

The current results reinforce the utility of qualitative approaches in studies of ADHD and sleep. Novel insights to emerge from the study include the perceived importance of the link between emotional and executive dysfunction and sleep problems, sleep hygiene practices and other steps parents report using to aid their children's sleep, and how children's sleep problems may act as a trigger for engagement with clinical services that ultimately lead to diagnosis of ADHD.

This study has further underlined the importance of parent perceptions and the steps they undertake to help alleviate the child's sleep problems. As such, the child's experience of sleep takes shape in the family, governed by their parents. In the next chapter we quantitatively explore the relationship between parent insomnia probability, presence of ADHD features and ADHD child's sleep problems.

Chapter 4:

Associations between sleep problems in children with ADHD and parental insomnia and ADHD symptoms.

Abstract

Sleep disturbances are common in children with attention deficit hyperactivity disorder (ADHD). Children's sleep problem may influence, and be influenced by, parents' sleep problems as well as parents' ADHD symptoms. In the current study we have examined the associations of parent-rated sleep quality and sleep timing of pre-adolescent children with parental insomnia symptoms, parental ADHD symptoms and dysfunctional attitudes and beliefs about sleep (N=120). Childhood sleep problems were common in the sample, with 82% of children exceeding the threshold for the presence of a paediatric sleep disorder. Children's sleep quality showed minimal association with their sleep timing and chronotype. Parental insomnia symptoms, ADHD symptoms and dysfunctional beliefs and attitudes about sleep all associated with their children's sleep quality, and with the child sleep subdomains of sleep anxiety and parasomnias. In multiple regression analysis, only the parental insomnia score was a significant predictor of children's sleep quality. Children's bedtimes, wake times, sleep duration, chronotype or social jetlag did not associate with parents' ADHD or insomnia symptoms. Sleep quality was significantly poorer in children whose parents scored both as consistent for adult ADHD (as per a screener tool) and probable for insomnia disorder compared to parents who scored as either ADHD consistent or insomnia probable, or those who parents scored as neither. We discuss the putative nature of the relationships between sleep quality of children with ADHD and parental ADHD and insomnia symptoms and suggest that clinicians consider parental sleep when attending to children with ADHD.

4.1 Introduction

Attention deficit hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder in children and young persons with an estimated prevalence of 7.2% (95% confidence interval: 6.7 to 7.8) (Wilcutt, 2012), characterised by the core symptoms of attentional difficulties, impulsivity and hyperactivity (Posner et al, 2020). Sleep problems are reported to be common in childhood ADHD, with 28-44 percent (Sung et al. 2008) of parents reporting that their children with ADHD experience sleep disturbances. These sleep disturbances may include long sleep-onset latency, delayed sleep phase, increased limb movements, daytime sleepiness, shorter sleep duration and difficulty initiating and maintaining sleep (Bondopadhyay et al 2022). Sleep problems and ADHD symptoms may have overlapped neurobiology. For example, changes in dopaminergic pathways are reported in both ADHD and sleep disorders, Couto et al 2010), as are neurocognitive features such as executive dysfunction concerns and inattention (Moreau et al 2013; Hansen et al 2013), and psychopathological manifestations including internalising and externalising behaviours (Accardo et al 2012; Hansen et al 2011). These overlapping facets may be the products of complex multifactorial and bidirectional relationships between sleep problems and ADHD symptoms (Lycett et al 2014; Raman and Coogan, 2019).

Sleep problems and ADHD in children have been reported to exert impacts on parental sleep, mental health, and the family context (Buxton et al, 2015). Sleep dysfunction in children with ADHD may also be associated with a decrease in parental wellbeing, and this in turn may decrease parents' ability to implement effective sleep management strategies for the child (Martin, 2019). Poorer sleep in adults is related to low mood (Konarski et al 2018), increased anger (Hisler & Krizan 2017) and increased stress levels (Da Estrela et al 2018), which all may impact on parenting behaviours and lead to poorer sleep health in the children (Bordeleau et al

2012). A bidirectional relationship between sleep and mental health issues can also be seen among the parent and child cohorts, with Children of parents with insomnia are reported to experience higher levels of sleep disturbances (Zhang et al 2010), as do children whose parents suffer from low mood (Meltzer &Mindell 2007). Further, as ADHD is a highly heritable condition (Freitag et al, 2010) and there is an elevated likelihood that parents of children with ADHD will themselves have undiagnosed ADHD (Waite and Ramsay, 2010); prevalence of ADHD in fathers and mothers of children with ADHD is 40%-50% elevated compared to the general population (Starck et al 2016). As sleep problems are common in adults with ADHD (Coogan and McGowan, 2017), it is of interest to explore the impacts of parent's ADHD-related sleep problems on their children's sleep.

In the current study we sought to explore whether parental insomnia symptoms, sleep beliefs and ADHD symptoms associate with sleep problems and features in their children with ADHD. While previous research has reported that parental sleep quality is associated with their child's sleep and ADHD symptom severity (Martin et al. 2021, Varma et al 2020 Martin et al. 2019), there are no reports of the relationship between parental sleep and ADHD symptoms, and how these interact and associate differentially with sleep characteristics of their children with ADHD. As such, a broad aim of the study is to contribute to the understanding of the family/household context of paediatric sleep complaints in ADHD. We hypothesised that greater parental insomnia and ADHD symptoms associate with greater sleep problems in children with ADHD.

4.2 Methods

Participants

The sample consisted of 120 parents currently residing in the Republic of Ireland. Inclusion criteria for the study was to be a parent of a child diagnosed with ADHD aged between 6 and 12 years old. Parents of children with a primary diagnosis of a neurodevelopmental or psychological disorder other than ADHD were not included in the study sample. Participants were recruited via purposive sampling through advertising on the online platform of an ADHD support group charity operating in Dublin (ADHD Ireland). The study was granted ethical approval from Maynooth University Research Ethics Committee.

Study Design and Measures

The study used a cross sectional design. On receiving written consent for participation, an initial demographic information form was completed by the participant (age and gender of child, age and gender of parent, parent's occupation, whether child is currently on ADHD medication). Following the above, all participants completed a questionnaire on the Qualtrics platform (a GDPR compliant online research platform) which included a series of validated psychometric instruments that are listed below.

<u>The instruments used for assessment of parental ADHD and sleep characteristics were:</u>

Adult ADHD Self Rating Scale v1.1 (ASRS). This is an 18 item self-report symptom screening checklist based on the ADHD DSM-IV criteria, where a subject responds to a particular statement by selecting one of the 5 response options ranging from 'never', 'rarely', 'sometimes', 'often' and 'very often' (Adler et al, 2006). It is important to note that ASRS is not a diagnostic tool, as it does not gather information regarding childhood presence of symptoms or the functional impact of the symptoms which are necessary to make a diagnosis. Four categories of scores were obtained from the ASRS. The first are two sets of scores for

Inattention and Hyperactivity/Impulsivity which are interpreted from the ASRS 18 item scores. These scores are divided into three categories, scores ranging from 0-16 (low ADHD related inattention/hyperactivity), scores ranging from 17-23 (moderate ADHD related inattention/hyperactivity) and scores ranging 24 or above (high ADHD inattention/hyperactivity). A total ASRS score derived from the 18 items of the scale ranging from 0 to 72 was calculated, and an ADHD consistency/inconsistency category is derived.

Dysfunctional Beliefs and Attitudes about Sleep-16 (DBAS) is a 16-item self-rating scale which was used to assess parents' sleep-related beliefs, as dysfunctional sleep beliefs have been strongly implicated in insomnia disorder (Morin et al, 2007). Each item is scored on a 10-point scale; the total score is calculated from all of the items on the scale, with higher scores representing more dysfunctional beliefs about sleep.

Sleep Condition Indicator (SCI) was used to assess the presence of insomnia symptoms and the probability of the presence of insomnia disorder in the parents. The SCI is an eight-item rating scale developed to screen for insomnia disorder based on DSM-5 criteria, and has been shown to have good psychometric properties (Espie, et al, 2014). Lower scores on the SCI indicate more insomnia symptoms and a total score of less than 16 indicated probability of insomnia disorder.

<u>The instruments used for the parental-rating of their children's sleep characteristics were:</u>

Child Sleep Habits Questionnaire (CSHQ): This is a 33-item parent report scale to assess the multidimensional sleep problems experienced by the child over the past 30 days (Owens, et al., 2000). Each item in the questionnaire is scored on a 3-point scale as occurring "usually" (i.e., 5–7 times within the past week), "sometimes" (i.e., 2–4 times within the past week), or "rarely" (i.e., never or 1 time within the past week). Factors of the scale are bedtime resistance, sleep onset-delay, sleep duration, sleep anxiety, night waking, parasomnias, sleep-

disordered breathing, and daytime sleepiness. A total CSHQ score of over 41 indicates a paediatric sleep disorder; scores of >41 identify 80% of children with a clinically diagnosed sleep disorder (Owens et al, 2000).

Sleep Disturbance Scale for Children (SDSC) is a 26-item parent questionnaire to assess the presence of sleep disorder features among children (Bruni et al. 1996). Apart from the first 2 sleep duration items, the next 24 items involve the parent choosing from one of the 5 options (Never, Occasionally, Sometimes, Often and Always) as comment for six domains including disorders of initiating and maintaining sleep, sleep breathing disorders, disorders of arousal, sleep-wake transition disorders, disorder of excessive somnolence and sleep hyperhidrosis are explored in this tool. Raw scores derived from each of the above domain is standardized as T-scores (Mean = 50, Standard Deviation = 10), with T-scores above 2 SD (i.e., 70T) considered clinically elevated.

Children Sleep Wake Scale (CSWS) is a 25 item parent-report scale to assess the behavioural sleep quality of the child (LeBourgeois and Harsh, 2016). It has a 5-factor structure: Going to bed, falling asleep, maintaining sleep, reinitiating sleep, returning to wakefulness. The average score of each subscale yields a total sleep quality score for the report.

Sleep Hygiene Inventory Paediatrics (SHIP) is a parent-rated 15 item questionnaire to assess sleep quality in children and adolescents and was developed originally for use in paediatric populations with chronic headache (Rabner et al., 2017). Respondents choose options on a 3-point Likert scale, scores ranging between 0-30, and higher scores signifying greater sleep disturbance.

Children's Chronotype Questionnaire (CCTQ; Werner et al, 2009) is an adaptation of both the Munich Chrono-Type Questionnaire (MCTQ; Roenneberg, 2004) and Morningness/ Eveningness Scale for Children (MESC; Carskadon et al., 1993) for use in pre-pubertal

children. Caregivers are asked to answer questions about sleep/wake timings on workdays (when the child has to go to school, weekdays) and free days (holidays, weekends, days where no scheduled activities are planned upon waking). Variables computed are the timing of mid sleep on free days (i.e., the midpoint of sleep on free days which signifies chronotype) and social jetlag (the difference between midsleep on free days and workdays). This scale also included Morningness and Eveningness scores that were derived from responses to 10 questions. Morning types were classified by a M/E scale score of ≤23, intermediate types by a score of 24–32, and evening types by a score ≥33.

While designing the questionnaire interface on the Qualtrics platform, we chose the questions to require mandatory responses from the participant. This meant the participant had to answer all questions in each section in order to proceed to the next. This helped eliminate missing responses from our data, however, did increase the likelihood of automatic/non read responding by the parent.

Data Analysis

After screening and cleaning to detect and remove invalid responses, scores from each scale were computed and the required total and sub-factor scores were collated in SPSS (IBM Corporation). Descriptive statistical analysis was completed for the data to generate means, standard deviations, percentage frequencies, and composite scores. Data was assessed for normality and presence of outliers using the Shapiro Wilk test and examination of histograms. Legitimate values which were noted as outliers through the Box blots were winsorized to 1 x the highest value in that distribution. Spearman's rank-order correlation coefficient was used to determine the relationship between continuous variables. Chi-square tests were used to assess associations between categorical variables. Mann-Whitney U and Kruskal-Wallis tests were used for groupwise comparisons when the dependent variable was not normally distributed, and t-tests and ANOVAs used for parametric data. Multiple linear regression was

conducted as a standard model following confirmation of the assumptions of homoscedasticity, normality of distribution of the residuals and lack of multicollinearity. $P<0.05$ was interpreted as indicating statistically significant differences and associations, and effect sizes were interpreted as per Cohen (1988).

4.3 Results

Descriptive statistics

Table 4.1 presents the demographic information on the children and parents in the study, and Table 4.2 shows descriptive statistics for the child and parent psychometric variables. From the CSHQ scores, 82.5% of children were identified as having a paediatric sleep disorder (total CSHQ score >41), and the frequency of such did not differ in different age categories (6-9 years old/10-12 years old) or by gender of the children (P=0.79 and P=0.322 respectively). Chi-square test for independence indicated a significant association between children's ADHD medication use and the presence of a sleep disorder ($\chi 2$= 4.93, P=0.032, phi=0.24); 40% of children identified as having a sleep disorder were not on medication whilst 60% were on ADHD medication. The Morningness-Eveningness categories (morning type (15% of children)/intermediate type (29% of children)/ evening type (56% of children)) did not differ significantly across age groups, gender, or ADHD medication status (P=0.271, P=0.44, P=0.391 respectively). Group differences by gender were found with female children having later Mid Sleep on Free Days (MsF) than male children (03:45 vs. 02:45, U=203, P=0.009, r=0.27 (small effect size)) and female children having greater social jetlag than male children (75 minutes vs 25 minutes, U=219.5, P=0.01, r=0.26 (small effect size)). Group differences by children's age category were also found for MsF (6-9 year old median=2:30, 10-12 year old median=3:34, U = 283, P<.01, r = .30 (moderate effect size)) and social jetlag (6-9 year old median=15 minutes, 10-12 median year old=60 minutes, U = 384.5, P< .05, r=.20 (small effect size)).

For parents, 36% had probable insomnia based on their SCI scores, and this insomnia probability did not differ significantly as per the parent's age group (29-39 years old vs. 40-54 years old) or gender (P=0.493, P=0.496 respectively). 35% of parents had scores on the ASRS screener consistent with the presence of ADHD features, and parental ADHD screener

consistency did not differ as per age group or gender (P=0.359, P=0.632 respectively). 22% of parents scored as being consistent with ADHD screener and probable for insomnia disorder, whilst 52% of parents scored as being neither ADHD-consistent or probable for insomnia disorder.

Table 4.1 *Demographics of the children and parents in the sample. Continuous variables are presented as means and standard deviation, and categorical variables are represented as frequency (percentages).*

Variables	Child	Parent
Age Mean (SD)	n-88 9.6 (1.96)	n-83 42.5 (5.50)
Age groups n (%)	6-9 40 (45.4%) 10-12 48 (54.5%)	29-39 18 (21.6%) 40-54 65 (78.3%)
Gender n (%)	n-89 Male 71 (79.7%) Female 18 (20.2%)	n-101 Male 7 (6.9%) Female 94 (93%)
Sleep time, Mean (SD)	n-89 Male 9:18 pm (1:07) Female 9:30 pm (1:04)	-
Wake time, Mean (SD)	Male 7:10 am (1:01) Female 7:39 am (0:48)	-
Sleep duration, Mean (SD)	Male 8.70 hrs (0.19 hrs) Female 8.97 hrs (1.51 hrs)	-
Parent profession n (%) Medical Non-medical	-	n-84 19 (22.6%) 65 (77.3%)
ADHD Medication Use Yes No	n-86 46 (53.4 %) 40 (46.5 %)	-

Note. SD = Standard Deviation

Table 4.2 *Child sleep questionnaire scores and parental scores for insomnia, ADHD symptoms and dysfunctional attitudes and beliefs about sleep.*

		Valid N	M (SD)	Minimum	Maximum
Child variables	CSHQ total	120	53.13(10.46)	33	81
	CSDS- T	94	76.17(17.70)	45	100
	CSWS total	115	3.05(0.88)	1.24	5.20
	SHIP score	115	12.76(6.04)	2	25
	SJ (mins)	94	46.71(41.93)	0	165
	MsF	91	3:02 (1:02) (AM)	1:07	5:30
	M-E score	96	33.34(8.38)	15	47
Parent variables	SCI total	91	19.08(8.55)	0	32
	DBAS total	90	4.35(1.88)	0.12	8.50
	ASRS total	93	29.61(16.64)	0	72

Note. M- Mean; SD- Standard Deviation; CSHQ- Child Sleep Habits Questionnaire total score; CSDS T-score – Child Sleep Disturbance Scale T-score; CSWS total- Child Sleep Wake Scale total score; SHIP score- Sleep Hygiene Inventory Paediatrics score; SJ mins- Social Jetlag in minutes; MsF- Mid sleep in free days; M-E score- Morningness-Eveningness score derived from the CCTQ; SCI score- Sleep Conditions Indicator score; DBAS score- Dysfunctional Beliefs About Sleep score; ASRS – Adult ADHD Self Report Scale total score.

Cross-correlation of children's scores on sleep instruments

We undertook a series of exploratory correlational analyses to compare scores on the different paediatric sleep scales used in the study (CSHQ, CSDS, CSWS, SHIP and CCTQ). Correlation analysis demonstrated a high degree of collinearity between the different paediatric sleep quality scales applied: CSHQ total scores showed strong correlation with the CSDS scores ($r=0.82$, $n = 94$, $P<0.001$), CSWS scores ($r=–0.78$, $n=115$, $P< 0.001$) and SHIP scores ($r=0.74$, $n= 115$, $P<0.001$). Therefore, for the next section of the analysis and for reasons of parsimony, we used the CSHQ as the measure of parent-rated child sleep quality. CSHQ total score had a moderate negative association with the child's sleep duration ($r=-0.38$, $n=120$, $P< 0.001$; Figure 4.1A). A moderate, positive correlation was found between CSHQ and the M-E score ($r=0.33$, $n=96$, $P<0.001$; Figure 4.1B). No statistically significant correlation was found for CSHQ total

score with children's MSF (r=0.140, n=91, P=0.186; Figure 4.1C) or social jetlag (r=0.123, n=94, P=0.238; Figure 4.1D). .

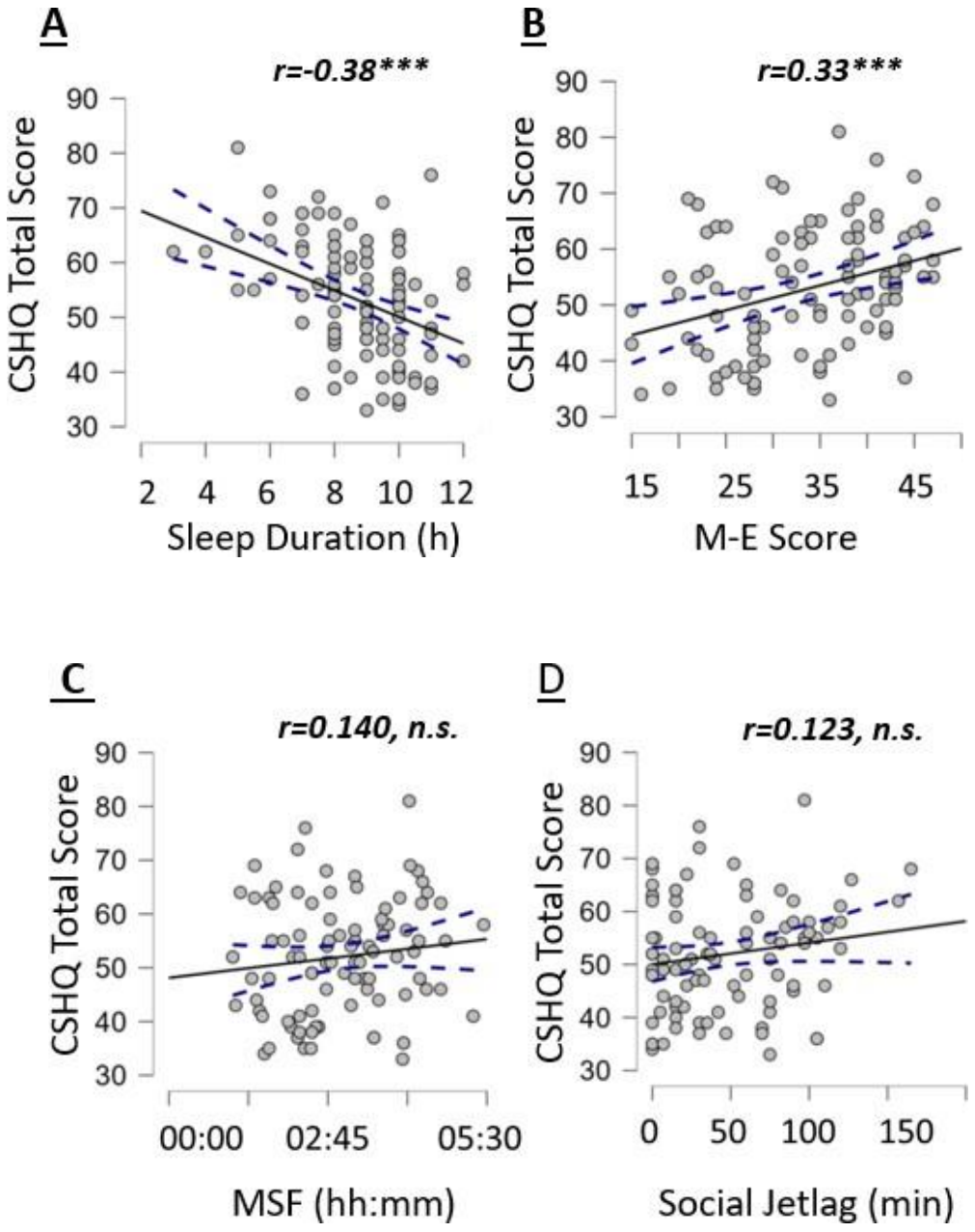


Figure 4.1: *Scatterplots showing the associations of children's total CSHQ scores and their (A) sleep duration, (B) M-E score, (C) MSF and (D) Social Jetlag. The filled line represents the regression line, and the dashed line the 95% confidence interval around it*

Associations of children's sleep with parents' insomnia and ADHD symptoms

Associations between children's CSHQ total score and parental insomnia symptoms from the SCI, dysfunctional beliefs and attitudes about sleep (DBAS) and ADHD symptoms from the ASRS were investigated and examined (Table 4.3). A moderate, negative relationship between children's CSHQ total score and parental SCI scores was found ($r=–0.35$, $P<0.001$; Table 4.3 and Figure 4.2A). There was also a small, positive association between children's CSHQ scores and parents' ASRS total scores ($r=0.28$, $P< 0.01$; Table 4.3 and Figure 4.2B). In addition to the ASRS total score, ASRS sub-scores for inattention ($r=0.23$, $P< 0.05$; Table 4.3), and hyperactivity ($r=0.33$, $P< .01$; Table 4.3) were associated with the CSHQ score. A small positive relationship was found between CSHQ total score and the parent DBAS score ($r=0.23$, $P<0.05$; Table 4.3 and Figure 4.2C). No significant associations were found between parent's SCI, DBAS and ASRS total scores with the children's bedtime, wake time, sleep duration, social jetlag, MSF and M-E scores (Table 4.3).

A linear multiple regression model was run with children's total CSHQ score as the dependent variable and parental total SCI, ASRS and DBAS scores as the independent variables. The model's adjusted R^2 was 0.137 and parental SCI emerged as the only independent variable whose β value was significantly different to zero ($\beta=-0.309$, $P<0.001$; Table 4.4). Therefore, although parent's screener-based ADHD features, sleep related dysfunctional beliefs (DBAS) and insomnia probability (SCI) were associated with the child's total seep problem score, parental insomnia probability emerged as the significant predictor variable for the child's sleep.

Table 4.3 *Correlations between child sleep variables and parental ASRS, SCI and DBAS scores. Values presented as Spearman rank correlation coefficients and their 95% confidence intervals.*

	SCI	ASRS	DBAS	ADHD I	ADHD H
CSHQ total	-0.353*** (-0.522 - -0.157)	0.289** (0.091-0.466)	0.233* (0.026-0.421)	0.238* (0.036-0.421)	0.332** (0.136-0.502)
Bedtime	-0.051 (-0.256- 0.159)	-0.051 (-0.253- 0.155)	-0.066 (-0.271- 0.146)	-0.026 (-0.229- 0.180)	-0.059 (-0.262 - 0.149)
Waketime	0.045 (-0.163- 0.250)	0.028 (-0.177- 0.230)	-0.079 -0.283- 0.131	0.084 (-0.122- 0.283)	-0.067 (-0.268- 0.140)
Sleep duration	-0.049 (-0.253- 0.160)	0.056 (-0.149- 0.257)	-0.066 -0.271- 0.144	0.108 (-0.098- 0.305)	-0.014 (-0.218- 0.191)
MsF	0.058 (-0.161- 0.272)	-0.018 (-0.230- 0.196)	-0.168 -0.373- 0.052	-0.059 (-0.269- 0.156)	0.030 (-0.185- 0.243)
Social jetlag	0.082 (-0.134 - 0.290)	0.042 (-0.169 - 0.249)	-0.189 (-0.388 - 0.026)	0.032 (-0.179- 0.240)	0.089 (-0.124- 0.294)
M-E score	-0.061 (-0.268- 0.152)	0.104 (-0.105- 0.305)	-0.017 (-0.228- 0.196)	0.081 (-0.128- 0.283)	0.131 (-0.079- 0.331)

Note. CSHQ- Child Sleep Habits Questionnaire total score; SJ mins- Social Jetlag in minutes; MsF- Mid sleep in free days; M-E score- Morningness-Eveningness score derived from the CCTQ; SCI score- Sleep Conditions Indicator score; DBAS score- Dysfunctional Beliefs About Sleep score; ASRS – Adult ADHD Self Report Scale total score. ADHD I – ASRS Inattention item scores total; ADHD H – ASRS Inattention item scores total. * denotes P< 0.05, ** P<0.01, *** P<0.001.

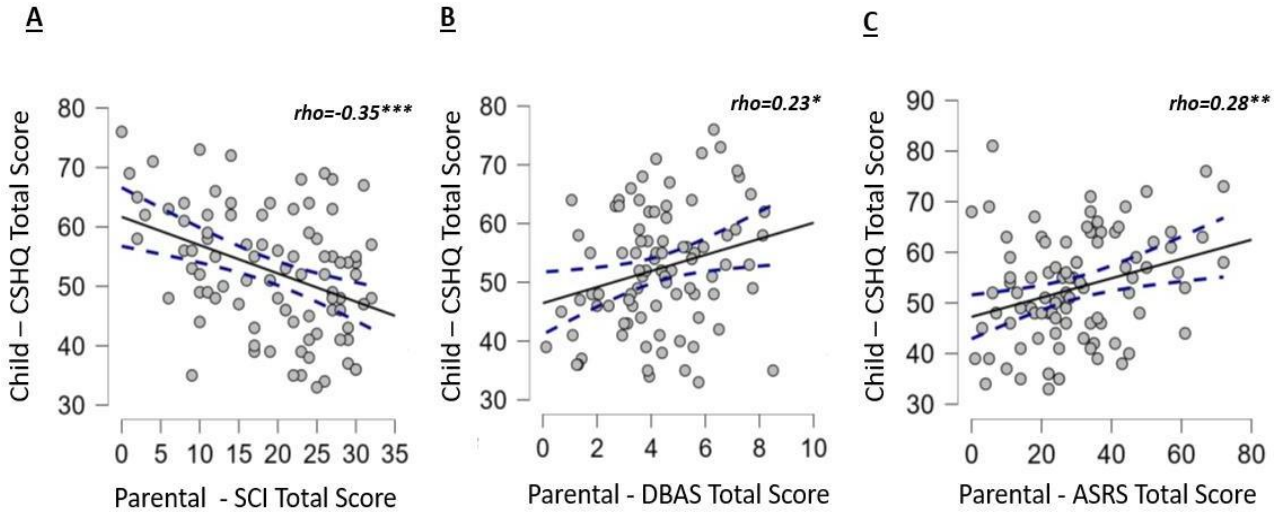


Figure 4.2: *Scatterplots showing the associations of children's total CSHQ with parental (A) SCI total scores, (B) DBAS total scores and (C) ASRS total scores. The filled line represents the regression line, and the dashed line the 95% confidence interval around it.*

Table 4.4: *Multiple regression model with total CSHQ score as the dependent variable, and parental SCI, ASRS and DBAS scores as the independent variables.*

Variable	Beta	t	Sig.
SCI	-.309	-2.36	0.021
ASRS total	0.112	0.388	0.348
DBAS	0.046	0.944	0.699

Note. Adjusted model R^2= 0.137, F=5.63, P < 0.001. SCI score- Sleep Conditions Indicator score; DBAS score- Dysfunctional Beliefs About Sleep score; ASRS – Adult ADHD Self Report Scale total score.

As children's CSHQ total scores were associated with parents' SCI and ASRS scores, we further examined the association of the CSHQ subscales with parental scores on the SCI and ASRS (Table 4.5). Parents' insomnia symptoms correlated statistically significantly with children's bedtime resistance (r=-0.23, P<0 .05), as did children's sleep anxiety (r=-0.29, P<0.01), night wakenings (r=-0.32, P< 0.01) and parasomnia scores (r=-0.29, P< .01; Figure 4.3A). Parents' total scores on the ASRS associated with children's sleep anxiety (r=0.28, P< 0.01) and parasomnia scores (r=0.30, P< .01; Figure 4.3B).

Table 4.5: *Correlations between children's CSHQ sub-scales and parental SCI and ASRS scores. Values presented as Spearman rank correlation coefficients and their 95% confidence intervals.*

	SCI	ASRS
Bedtime Resistance	-0.237* (-0.425- -0.029)	0.167 (-0.040 - 0.361)
Sleep Onset Delay	-0.066 (-0.271- 0.146)	0.141 (-0.067 - 0.337)
Sleep Duration	-0.117 (-0.319 - 0.094)	0.065 (-0.143 - 0.267)
Sleep Anxiety	-0.418*** (-0.577- -0.228)	0.285** (0.084 - 0.464)
Night Waking	-0.329** (-0.504- -0.128)	0.164 (-0.043 - 0.358)

Parasomnia	-0.299** (-0.478- -0.095)	0.307** (0.107 - 0.482)
Sleep Disordered Breathing	-0.151 (-0.349- -0.061)	-0.007 (-0.213 - 0.199)
Daytime Sleepiness	-0.073 (-0.278- 0.139)	0.106 (-0.102 - 0.305)

Note. * denotes P< 0.05, ** P<0.01, *** P<0.001. SCI score- Sleep Conditions Indicator score; ASRS – Adult ADHD Self Report Scale total score.

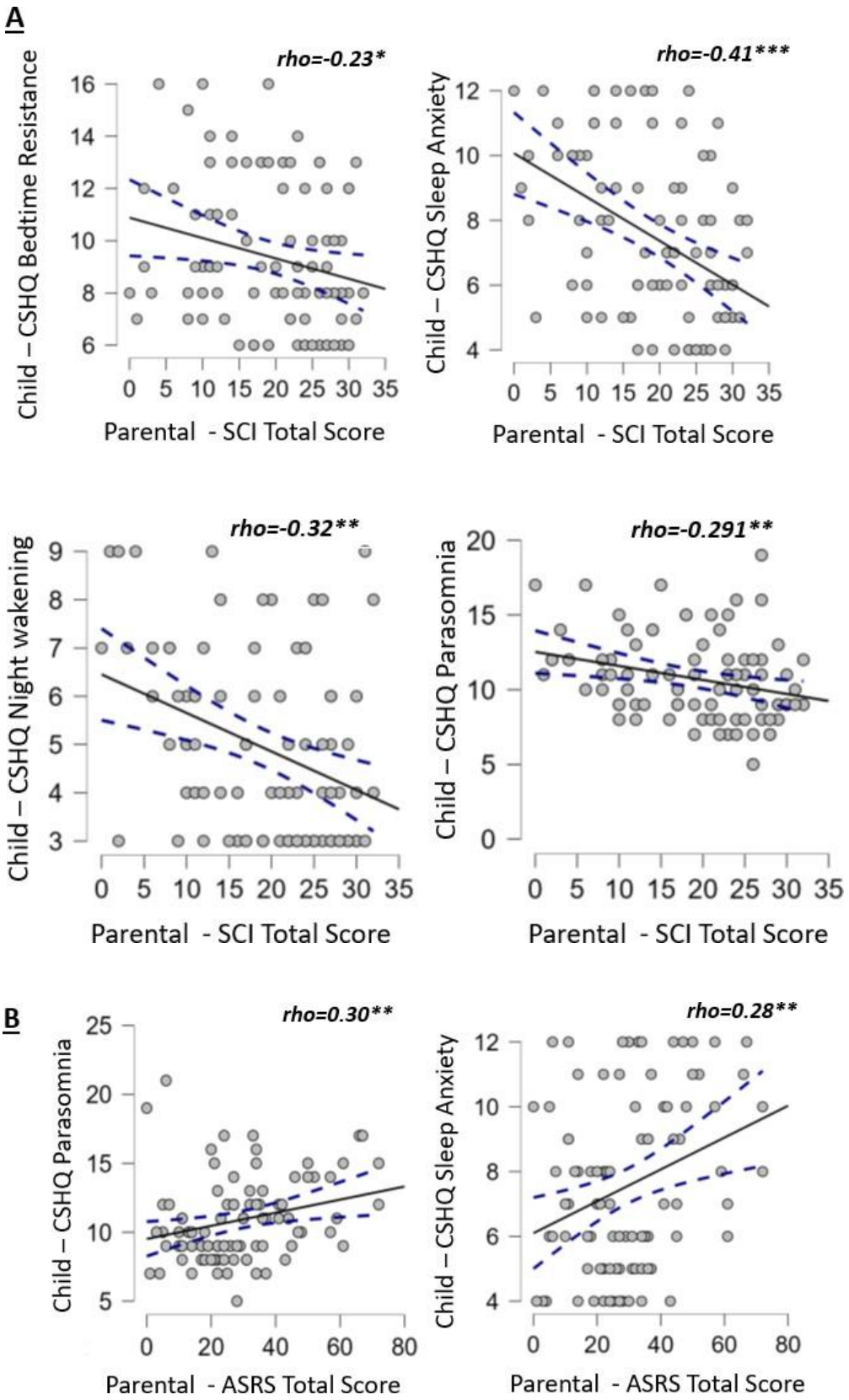


Figure 4.3: *Scatterplots showing the associations of children's CSHQ subscales scores with (A) parental SCI and (B) ASRS scores. The filled line represents the regression line, and the dashed line the 95% confidence interval around it.*

To further examine the relationships between child and parental scores, we undertook groupwise analysis of children's sleep features according to parental grouping based on cut-off points for probable insomnia and ADHD-consistency. Those children with a parent who had ADHD-consistent score did not have higher total score on the CSHQ compared to children whose parents did not have an ADHD-consistent ASRS score (consistent, n=32, CSHQ mean=55.4$\pm$1.8 vs inconsistent, n=60, CSHQ mean=51.1$\pm$1.1, P=0.066; Figure 4.4A). Children whose parents' SCI scores indicated probable insomnia disorder had higher CSHQ scores than children whose parents did not have probable insomnia disorder (probable insomnia group, n=32, median CSHQ=58 vs. improbable group, n=58, median CSHQ=48.50, P< 0.001, r= 0.35 (moderate effect size); Figure 4.4B). Hence, group comparisons again validated differences in child's sleep problem scores based on parent's level of insomnia probability, and not as per their ADHD (screener based) consistency.

Children's sleep duration varied according to parental ADHD-consistency (9.34h$\pm$0.31h vs 8.45h$\pm$0.21h, P<0.05; Figure 4.4 C) but did not vary according to parental probable insomnia grouping (8.74h+0.24 vs 8.72+0.34, P=0.95; Figure 4.4 D). Children's M-E scores did not vary significantly according to whether their parents were either ADHD-consistent/inconsistent (P=0.71; Figure 4.4E) or probable/improbable insomnia disorder (P=0.14; Figure 4.4F; MSF or children's social also did not differ according to parental groupings, data not shown).

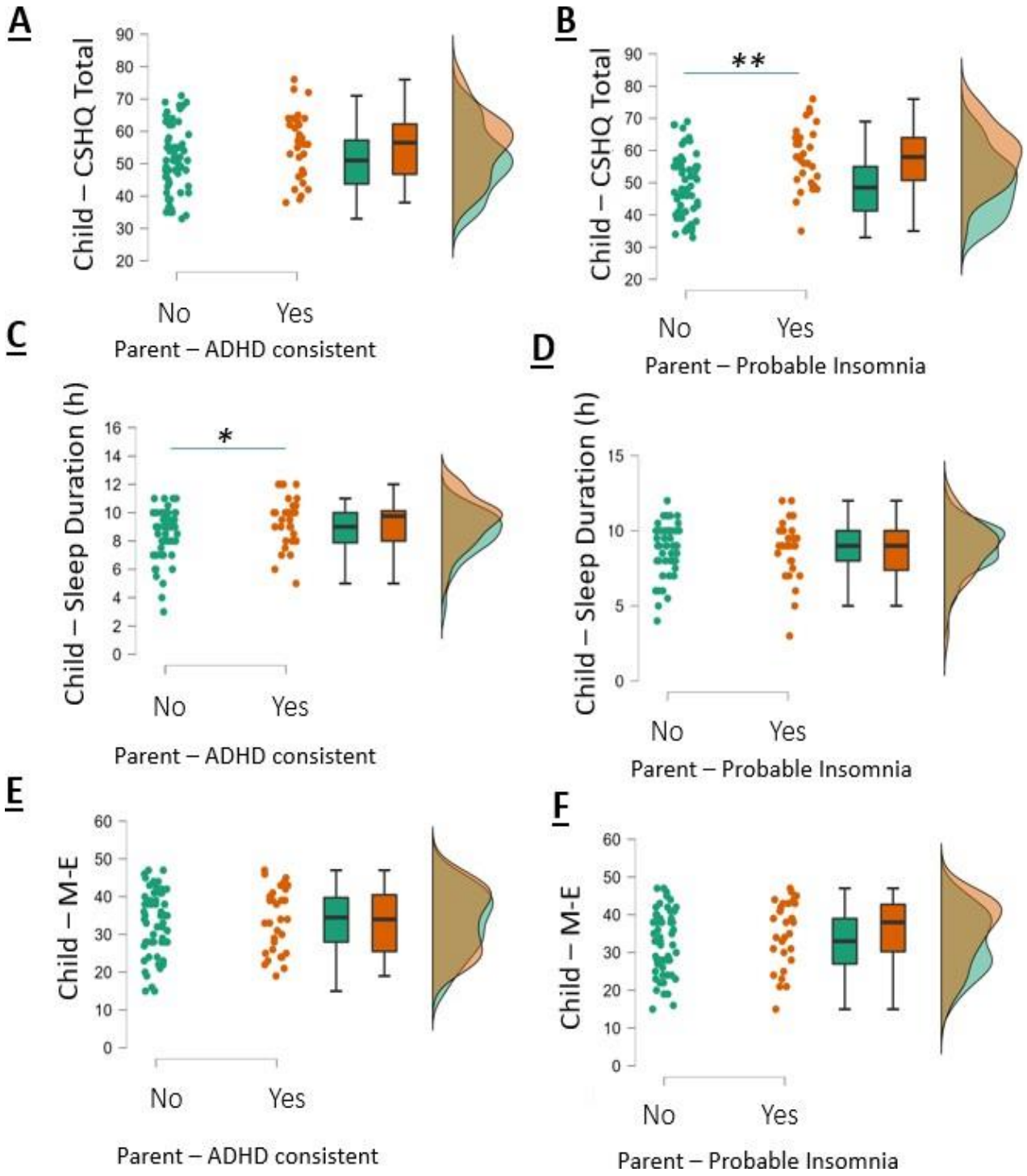


Figure 4.4: *Raincloud plots showing groupwise comparisons of children's total CSHQ scores according to parents' ADHD consistency from ASRS scores (A) and insomnia probability from SCI scores (B), children's sleep duration with parental ADHD-consistency (C) and insomnia probability (D), and children's M-E scores with parental ADHD-consistency (E) and insomnia probability (F). ** denotes P<0.01 and * P<0.05 by independent t-test.*

Children of parents who were both ADHD-consistent and probable for insomnia disorder showed significant worse sleep quality than children whose parents were ADHD-inconsistent and insomnia improbable, and those whose parents were either ADHD-consistent or insomnia probable ($F(2, 87)=8.2$, $P<0.001$; by Tukey post-hoc test $P<0.001$ between children of parents who were both ADHD-consistent and probable for insomnia disorder and children whose parents were ADHD-inconsistent and insomnia improbable, $P<0.01$ between children of parents who were both ADHD-consistent and probable for insomnia disorder and children whose parents were either ADHD-consistent or insomnia probable; Figure5).

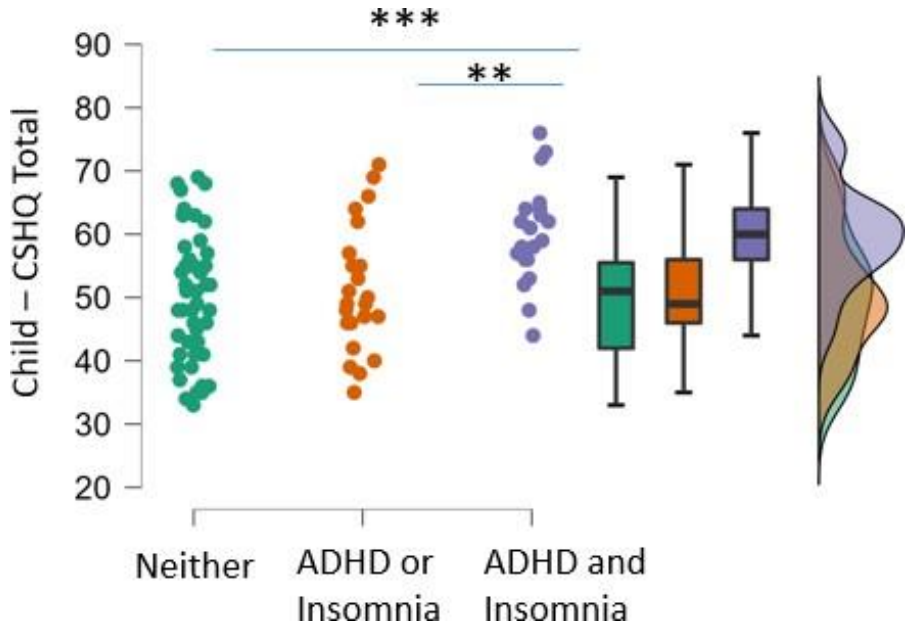


Figure 4.5: *Raincloud plots showing groupwise comparisons of children's total CSHQ scores according to parents' combined status of ADHD consistency and insomnia probability. *** denotes P<0.001 and ** P<0.01 by Tukey post-hoc test following one-way ANOVA.*

4.4 Discussion

The current results show that sleep problems in children with ADHD are associated with parental symptoms of ADHD and insomnia, and that parental insomnia symptoms are the strongest independent predictor of the severity of children's sleep problems. Sleep problems were prevalent in the children in the study, with 82% of children exceeding the threshold for the presence of a paediatric sleep disorder. The children of parents who were scored as both ADHD-consistent and insomnia disorder probable showed greater sleep problems than children of parents with only one of ADHD-consistency or insomnia probability, or who were neither ADHD-consistent or insomnia probable, thereby demonstrating the additive effect of each condition on the child's sleep. Considering specific sleep problems, children's sleep anxiety and parasomnia scores associated with both parental ADHD and insomnia symptoms, but sleep disordered breathing, daytime sleepiness and sleep onset delay were not. Parents' ADHD and insomnia symptoms did not associate with children's bedtimes, wake times, sleep duration, social jetlag or chronotype.

Sleep problems are common in both childhood and adult ADHD (Bondopanhyay et al, 2022; Coogan and McGowan, 2017), and sleep problems in ADHD may be influenced by the severity of symptoms, ADHD subtype, comorbid conditions, and specific neurocognitive deficits (Mayes et al. 2009, Schneider et al. 2016, Eyuboglu and Eyuboglu, 2017) as well as factors such as socioeconomic circumstance and medication (Bagley et al. 2015). There is a marked paucity of literature on the relationship between children with ADHD sleep problems and parental sleep and ADHD symptoms. Only two studies explored the above relationship, with Bar and colleagues (2016) reporting that parental sleep quality (assessed through the Pittsburgh Sleep Quality Index) was predicted by the children's pre-sleep arousal score and their anxiety; and Matsouka and colleagues (2014) who showed that parental sleep quality (also

assessed through the Pittsburgh Sleep Quality Index) associated with total sleep problem scores in a small sample of Japanese children with pervasive developmental disorder or ADHD.

There is evidence for household impacts of children's sleep problems in ADHD, which are associated with poorer parental mental health and higher parenting stress (Martin et al. 2019). Improvement in parental anxiety is reported to result from behavioural intervention for children's sleep problems associated with ADHD (Sciberras et al 2011). Lack of consistent daily routines has previously been reported to predict increased bedtime resistance for children with ADHD (Noble et al 2011), and interventions for better sleep hygiene and parenting consistency decreased bedtime resistance in this population (Sciberras et al 2017). Such previous findings may be consistent with our current report that children's bedtime resistance, night waking, parasomnias and sleep anxiety are significantly correlated with parental insomnia probability, as insomnia disorder is associated with greater sleep timing variability and less consistent sleep routines (Buysee et al, 2010; Rosler et al, 2022). As such, greater parental insomnia symptoms may result in less-consistent household bedtime routines which in turn contribute to children's bedtime resistance, sleep anxiety and even night-time wakenings. Further, as Noble et al (2011) report that parenting stress predicts children's sleep anxiety, and parenting stress may be associated with parental insomnia (Byars et al, 2011), parents' insomnia symptoms may contribute to greater parenting stress which in turn contributes to children's sleep problems. Indeed, a recent study has suggested a causal link between parental insomnia and children's insomnia during the early phase of the Covid-19 pandemic (Zhan et al, 2022). Conversely, children's sleep problems may contribute to parental insomnia symptoms: children with ADHD are reported to have higher sleep anxiety and more frequent night waking (Hansen et al 2011), with 22% needing a parent present in the bedroom to go to sleep (Arman et al 2011). As such, children's sleep problems and the attendant demands on parents may contribute to parental sleep problems.

Parents' self-reported ADHD symptoms were also associated with children's sleep problems, although in the regression model only insomnia scores emerged as a significant predictor of children's sleep problems in the regression model applied. Insomnia is common in adults with ADHD, with reported prevalence in the range of 43%-80% (Wynchank et al, 2017). As such, it is not immediately clear from the current result what impacts parental ADHD symptoms may exert on children's sleep independent of parental insomnia symptoms. It is of note that the current results indicate that sleep problems were more severe in children whose parent had both probable insomnia and were ADHD-consistent compared to children whose parent was either ADHD-consistent or insomnia probable, suggesting an additive effect/impact of ADHD- and insomnia-symptoms. Features of adult ADHD, such as alterations in time perception, stress and coping strategies may be salient for understanding how parental ADHD may contribute to less optimal children's bedtime routines and sleep habits (Weissenberger et al, 2021; Barra et al, 2021); however, further work is needed to clarify which, if any in particular, parental ADHD traits are most associated with children's sleep problems.

Parental expectation of their child's sleep duration has been found to affect the number of hours their children slept (Jarrin et al. 2020). Bessey et al. (2013) examined parental attitudes and beliefs about their ADHD child's sleep compared to those held by parents of typically developing children and found that parents of children with ADHD reported their child's sleep problems to be less modifiable and responsive to change. In line with the above, in our study we report that that higher levels of parent's dysfunctional sleep related beliefs were associated with them rating more sleep problems for their child. However, such dysfunctional attitudes and beliefs about sleep are common in insomnia disorder (Thakral et al, 2020), and parental DBAS scores did not emerge as a predictor of children's sleep problems independent of insomnia symptoms in the current study; therefore it is not clear from the current results if parental sleep beliefs independently influence children's sleep.

The current study design means that the directionality of associations between children's sleep problems and parental sleep and ADHD symptoms cannot be ascertained. It seems reasonable to assume that children's sleep problems (bedtime/sleep onset and/or sleep maintenance problems) could impact on parents' sleep routines and quality, and resulting parental sleep problems could increase the expression of ADHD-like impairments in executive function (Raman and Coogan, 2019). Another important point to consider is the potential for shared biological propensity towards ADHD symptoms and sleep problems in parents and children, as ADHD is a highly heritable condition (Posner et al, 2020). Recent evidence has suggested that sleep disturbances in ADHD could emerge due to overlapping genetic predispositions for ADHD and sleep problems (Gregory et al. 2017; Demontis et al. 2019; Akingbuwa et al. 2020; Takahashi et al. 2020) and ADHD polygenic risk scores were found to be associated with excessive somnolence and difficulty initiating sleep among children in the general population (Ohi et al. 2021). However, a recent study using a method to determine whether common genetic variant liability for specific traits are over or under transmitted from parents to children found that children with ADHD do not over-inherit or differentially inherit polygenic liability for longer sleep duration, insomnia or chronotype (Lewis et al. 2021).

When examining within-child associations, we note high levels of correlation on global scores on the paediatric sleep scales used. This is in line with the findings of Spruyt and Gozal (2011) who note a high level of shared/generic features among paediatric sleep psychometric instruments. However, we felt it important to test this assumption in the current paediatric ADHD sample. We chose to utilise the CSHQ scales for most of our analyses as it is well established and has been previously deployed in paediatric ADHD populations (eg. Bar et al, 2016; Matsouka et al, 2019). We found an association between CSHQ and M-E scores, but not between CSHQ and MSF or SJL scores; as such, it is not clear from these findings if poorer child sleep in ADHD is associated with greater evening orientation. ADHD, and ADHD

symptom severity, in adults is consistently found to be associated with evening preference/later chronotype (Coogan and McGowan, 2017), and later chronotype in adults is associated with poorer sleep quality (Raman and Coogan, 2020). However, the current sample was a pre-adolescent one, and given that adolescence is associated with profound changes in chronotype (Roenneberg et al, 2007), it may be that associations between later chronotype and sleep quality in ADHD emerges only during adolescence. Finally, we found that children's medication status was associated with sleep problems, a finding that has been commonly reported in previous studies (Bondopandhyay et al, 2022).

Strengths and Limitations

The current study has some important strengths. We deployed a number of assessments of paediatric sleep quality in the sample, to allow for a robust assessment of sleep issues in the current sample of children with ADHD. Further, we employed well-validated and clinically-relevant measures of parental sleep problems and ADHD symptoms. The combination of measures of ADHD and insomnia in the parents of children with ADHD has not been deployed previously in the examination of links between parental traits and children with ADHD's sleep problems. This is a pertinent issue to address, given both the high prevalence of sleep problems in ADHD and the high heritability of ADHD. The study also has some limitations. The assessment of children's sleep was solely dependent on parental report through psychometric instruments, and future work should seek to include direct objective assessment of children's sleep in the home setting. Moreover, because only one parent completed the questionnaire, the perspectives of the second parent (or another major guardian figure at home) remained unheard. The nonresponding parent/guardian might have details of the child's behavioral issues, cognitive difficulties and social interaction problems which in turn effects their sleep wake behaviors. Future studies should include two versions of the same questionnaire given to both parents/ or guardians in the household to capture a comprehensive account of the

child's sleep difficulties. Also, mandatory responses on survey questionnaire could increase the likelihood of parents responding without reading the full question statements. No clinical information on the severity of children's ADHD symptoms, nor on the subtype of ADHD, was gathered. Further, no information on comorbidities of ADHD in either parents or children were assessed; as such comorbidities arecommon in ADHD (Posner et al, 2020) and may impact on sleep characteristics, there is potential for differential findings in the presence or absence of such comorbidities. The neurobehavioral systems underlying arousal and emotion, and those involving sleep are shared (Dahl, 1996; Walker, 2009). Therefore, a major confounding variable for the results in this study could be specific difficulties with the child's temperament (Hayes et al, 2011) and genetic factors (Bouvette-Turcot et al 2015), that might affect both their sleep and emotional/behavioural regulation. In addition, parent's own mental health, level of stress and bedtime behaviors could also impact their perception of their child's sleep problems (Cook &Wiggs, 2022), thereby adding on as a confounding factor. Finally, thecurrent study was conducted during the Covid-19 pandemic. Given that 34% of parents previously reported worsening in their ADHD children's wellbeing during lockdown, whilst 31% reported that their children were doing better (Bobo et al 2020), it is unclear to which extent the current findings may have been influenced by the pandemic, although it is worth noting that schools were open and operating as per usual in Ireland during the period of data collection.

Conclusion

The current study indicates significant associations between sleep problem severity in children with ADHD and their parents' insomnia and ADHD symptoms. We suggest that clinicians working with families with children with ADHD may direct some attention to assessing both the children's and parents' sleep and offer whole-household guidance on promoting healthy sleeping habits.

Within the childhood ADHD clinical picture it is clear that parental and child's sleep functioning might have a bidirectional association which is characterised by the child's cognitive, behavioural and emotional functioning on the one hand and the parent's own sleep and mental health on the other hand. Acknowledging the unique features of the above association calls for an ADHD specific assessment of sleep functioning in children, which is the next step we took in Chapter 5.

Chapter 5:

A tool for assessing parental report of sleep for children with ADHD – Development of the Childhood ADHD Sleep Scale (CASS).

Abstract

This study presents initial psychometric analysis of the Childhood ADHD Sleep Scale (CASS), a parent-reported questionnaire to assess sleep problems in children with Attention Deficit Hyperactivity Disorder (ADHD). The unreduced CASS produces total score and five domain scores (Bedtime, Sleep Quality, Behaviours in Sleep, Daytime Functions and Impacts on family), in addition to sleep onset and wake time of the child on school days and holidays and parental perception about the impact of ADHD medication on sleep. 107 parents of children 6-12 years (with ADHD=59, children without ADHD = 48) residing in the Republic of Ireland completed the CASS survey on time 1 and time 2 (2 weeks later). All domain scores for the CASS differed across the ADHD and non-ADHD scores, (apart from the Daytime functions score, P = 0.074) and no scores differed across the medicated and non-medicated ADHD group. The original CASS demonstrated excellent internal consistency (α= 0.91) and the alpha coefficients for individual domains ranged from acceptable to good level (combined sample, range = 0.68- 0.91; ADHD sample, range = 0.60 – 0.86; non-ADHD sample, range = 0.63- 0.92). Test-retest reliability of the scale was acceptable (combined sample, range = 0.62- 0.86; ADHD sample, range = 0.56 – 0.78; non-ADHD sample, range = 0.60- 0.87). An exploratory factor analysis of the original CASS items led to the development of the Reduced CASS with 4 factors (Sleep Problems and Impacts, Executive and Sensory Regulation, Daytime Functions, and Parasomnias), demonstrating good internal consistency (α= 0.89). The reduced CASS also showed alpha coefficients for individual factors ranged from good to excellent level (combined sample, range = 0.74 – 0.91; ADHD sample, range =0.62 – 0.87; non-ADHD sample, range =0.74 – 0.91). Test-retest reliability of the scale was good (combined sample, range = 0.72 – 0.83; ADHD sample, range =0.64 – 0.84; non-ADHD sample, range =0.64 – 0.88). All factors of the reduced CASS differed across the ADHD and non-ADHD scores, (apart from the Daytime functions score, P = 0.21) and no scores differed across the

medicated and non-medicated ADHD group. The benefits of using a condition specific sleep assessment tool and the reduced CASS's utility in ascertaining sleep problems in the ADHD clinical picture are discussed.

5.1 Introduction

Clinical evaluation of a child diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) through neuropsychological tests reveal developmental concerns with various executive functions, processing speed, significant difficulty in paying selective and/or sustained attention/attentional switching and a lack of age-appropriate behavioural inhibition (Wu et al. 2022). The above are coupled with consequential difficulties in academic and social functioning (Langberg et al. 2013; Kofler et al. 2018). A majority of these disturbances manifest themselves in day-to-day functioning, including sleep/wake patterns (Hvolby, 2015). Co-occurrence of sleep concerns and ADHD reflect their prevalence in a pronounced way, with 70 % of individuals with ADHD having sleep related concerns (Yoon et al 2012) as opposed to 20-30 % in the general population (Quach et al 2012). Existing literature demonstrates that sleep disturbances in this population, including long sleep latency, sleep phase latency syndrome, increased periodic limb movements during sleep, daytime sleepiness, altered total sleep duration and difficulty initiating and maintaining sleep (Ball, 1997; Corkum et al., 1998; Cortese et al., 2006; Konofal et al., 2001, 2010; Mayes et al., 2009).

Further, sleep problems may be part of ADHD's symptomatology (Raman & Coogan, 2019). Quality sleep can facilitate memory consolidation and learning, as memories become resistant to attentional deficit related interference (Rasch and Born, 2013). Both in general population and ADHD cohorts sleep deprivation in children has been associated with greater variabilities in attention and vigilance tasks (Gruber et al. 2011; Lee et al. 2014; Kirszenblat and Swinderen, 2015; Lo et al. 2016; Killgore, 2010; Sciberras et al. 2015), in addition to increased executive function deficits (Lam et al 2011; Floros et al 2021). Additionally a range of psychological consequences are associated with sleep restrictions, including internalizing and externalizing behaviours and lack of ability to adapt to challenging social situations (Kahn et al 2013; Baum et al 2014). Children with ADHD, who already have a range of comorbid

behavioural and psychological concerns (Becker et al 2016; Smalley et al 2007), may experience exacerbation of these symptoms as a result of accompanied moderate to severe sleep problems (Lycett et al 2015). Moreover, sleep problems in children with ADHD are associated with poorer family outcomes (parental mental health, work attendance, quality of life, and reduced family wellbeing) (Lycett et al. 2016; Sung et al. 2008). Therefore in ADHD symptomatology, sleep plays a crucial role of exacerbating neurocognitive, behavioural and resultant functional symptoms and needs special attention both in case of research and clinical practice. Bondopadhyay et al., (2021) reviewed 148 studies investigating sleep in childhood ADHD which employed subjective assessment methods such as caregiver/teacher rated standardized scales and objective sleep/wake assessment methods such as polysomnography, actigraphy or physiological examination of bodily functions; and concluded that sleep disturbance may represent a clinically important feature of ADHD in children, which might be therapeutically targeted in a useful way.

Owing to the bidirectional association between sleep problems and ADHD symptoms (Gosling et al 2022; Quach et al 2018), careful assessment and sleep targeted interventions appear relevant for the clinical management of ADHD. Becker (2020) in their literature review conceptualised ADHD as a 24 hour disorder: just as ADHD clinical features interact with the child's day-time functional outcomes, they also interact with the child's sleep and sleep related functions producing distinct social/emotional/behavioural impacts, thereby marking sleep as a worthy target for intervention.

Sleep Assessment

Precise assessment of sleep disturbances in children with ADHD includes a range multidimensional means ranging from objective measures such a polysomnography, which records physiological changes occurring during sleep to ascertain sleep staging, respiration,

limb movements and the presence of sleep disorders (Marcus , 2001), or actigraphywherein the body's motor movements are recorded via actimetry sensors (Acebo et al. 1999), to subjective measures such as parent or child report questionnaires, which primarily provide retrospective account of the child's sleep over a particular time period (for example, within the last 1 week or 1 month). Information regarding the child's sleep and bedtime actions can also be gathered via sleep diaries which include nightly logs of the child's sleep and wake timings, sleep duration, antecedents, behaviours and consequences during and before bedtime (Hodge et al. 2012; Johnson et al 2012). Parent/caregiver questionnaires form a crucial component for the child's sleep related behavioural and observed physiological assessment, such as daytime sleepiness, sleep hygiene and sleep habits, attitudes and cognition about sleep, reported sleep timing and duration, measures related to sleep initiation and maintenance, reported physiological measures for example disordered breathing, limb movement during sleep, snoring and parasomnias (Lewandowski et al. 2011).

For use with paediatric populations, measures such as the Children's Sleep Hygiene Scale (Harsh et al 2002), the Family Inventory of Sleep Habits (Malow et al. 2009) and the Bedtime Routines Questionnaires (Henderson and Jordan, 2010) aim to ascertain sleep habits and hygiene (for example, bedtime routines, sleeping environment or activities before sleep). On the other hand, measures such as the Child Sleep Wake Scale (LeBourgeois and Harsh, 2001), the Sleep and Settle Questionnaire (Matthey, 2001), and the Tayside Sleep Questionnaire (McGreavey et al 2005) aim to measure the facets of sleep initiation and maintenance (for example, sleep onset, duration, disruptions and the quality of sleep). The Dysfunctional Beliefs about Sleep Questionnaire (Morin et al 1993) and the Presleep Arousal Survey for Children (Gregory et al 2008) aim to assess sleep related beliefs and attitudes, while daytime sleepiness (including wake time drowsiness, need to sleep and feeling tired) is measured via tools like Epworth Sleepiness Scale (Melendres et al. 2004) or Pediatric Daytime

Sleepiness Scale (Drake et al. 2003). In addition to the above measures, multidimensional tools such as Child Sleep Habits Questionnaire (Owen et al 2000), Paediatric Sleep Questionnaire (Chervin et al 1997) and Sleep Disturbance Scale for Children (Bruni et al. 1996) assess a broad range of physiological as well as behavioural sleep facets. Sen and Spruyt (2020), reviewed 70 tools evaluating sleep in children between 6-17 years via parental reports. They observed that more than half of the tools assessed general sleep health, and sleep tools designed for specific populations such as developmental disabilities is lacking. Additionally, they pronounced the need for tools assessing sleep routines, regularity of sleep patterns and the sleep in the context of treatment.

A tool for a clinical population

The above-mentioned tools were designed for use with general pediatric populations and are not specific to clinical populations, with the exception of a few. For example, the Family Inventory of Sleep Habits (FISH) (Malow et al 2009) and the Modified Simonds and Parraga Sleep Questionnaire (MSPSQ) (Simonds and Parraga, 1982, Wiggs et al 1996; Wiggs et al 1997) was found relevant to assess sleep in children with Autism Spectrum Disorder (ASD) (Johnson et al 2012). The FISH tool has autism specific items; for example sleep habit questions incorporate the child's comfort associated with optimal tactile sensation by querying about sleeping in certain fabric pyjamas or a comfort object. Although general pediatric sleep tools such as the CSHQ has been widely used in research for ASD cohorts, a questionnaire like FISH or MSPSQ demonstrates stronger potential for use with clinical populations as they address sleep disturbance which is specific to ASD clinical picture (Johnson et al 2012). For example CSHQ questionnaire for parasomnias is, 'Child awakens during the night screaming, sweating and inconsolable' while that for MSPSQ is related the ASD clinical picture, 'wakes during night screaming in terror', 'anxiety may be so bad that sweating, gasping and trembling

might happen'. These details help assess the condition specific sleep problems as well as ascertain the severity and impact of the core and comorbid symptoms of the condition.

Similarly, for assessing reported sleep functions among ADHD children, in addition to generalised widely used multidimensional tools (such as Childhood Sleep Habit Questionnaire, CSHQ; Owen et al, 2000), an ADHD specific sleep measure will more precisely gauge the nature of sleep related problems exclusively related to the child's ADHD symptomatology. Currently there is no sleep questionnaire for specific use with ADHD children. Such a measure could gather information which could be incorporated within the child's diagnostic formulation (for example the bio-psycho-social predisposing, precipitating and perpetuating factors of sleep problems) and in turn will make it possible for the clinicians to address them in subsequent therapeutic and pharmacological interventions.

We propose the need to develop a psychometric instrument designed specifically to assess sleep problems in pre-adolescent children with ADHD. We propose that the development of a new scale could be clinically impactful, especially considering that ADHD has an estimated prevalence of ~5% in pediatric populations. Therefore, wepropose a novel tool: the Childhood ADHD Sleep Scale (CASS) to assess parental report of sleep related behaviors and functions in children diagnosed with ADHD. In the CASS, we aim to capture areas of bedtime related pre-sleep emotions and behaviours, sleep quality, behaviors in(during) sleep, daytime functions and impacts on family. In addition, descriptive adjuncts of sleep impacts on medication use and details on sleep timing will be used to evaluate sleep timing and duration on school days and school-free days. We will cross-validate the CASS against a widely used existing measure (Child Sleep Habits Questionnaire, (Owen et al., 2000).

5.2 Materials and Methods

Participants

The sample consisted of 107 parents currently residing in the Republic of Ireland. Inclusion criteria for the study was to be a parent of a child diagnosed with ADHD (clinical group) or with no known diagnosis of a neurodevelopmental disorder (control group), aged between 5 and 12 years. Within the clinical group, parents of children with a primary diagnosis of a neurodevelopmental or psychological disorder other than ADHD were not included in the study sample. Participants were recruited via purposive sampling through advertising on the online platform of an ADHD support group charity operating in Dublin (ADHD Ireland). The study was granted ethical approval from Maynooth University Research Ethics Committee. Participating parents were remunerated with an online store gift card.

Study Design and Measures

This is a tool development study to assess the psychometric properties of a sleep questionnaire designed specifically for use with childhood ADHD populations. On receiving written consent for participation, an initial demographic information form was completed by the participant (age and gender of child, age and gender of parent, whether child is currently diagnosed with ADHD or is on prescribed ADHD medication). Following the above, all participants completed a questionnaire on the Qualtrics platform which included the psychometric instruments mentioned below. Two weeks after completing the first set of questionnaires, participants were sent a second questionnaire consisting only the novel tool (CASS) with the aim of conducting test-retest analysis of scores. After completion of the questionnaire, parents were briefed about the study variables and links were shared for parents to learn more about sleep in children.

Childhood ADHD Sleep Scale (CASS)

Below we describe the domains to be covered in the novel sleep questionnaire, the Childhood ADHD Sleep Scale (CASS).

The "Bedtime" domain includes the child's pre-sleep behaviours, need for specific persons or environments during sleep and their emotional reactions during bedtime. Literature has consistently demonstrated the presence of bedtime resistance, difficulty with sleep onset, restlessness during sleep (Corkum et al 2001; Gruber et al 2012, and Akinci et al 2015), and emotional problems resulting from comorbid anxiety or depression symptoms causing increased Sleep onset delay and shorter sleep duration (Moreau et al 2013; Mayes et al. 2009). In our qualitative study assessing sleep in children with ADHD via parental semi structured interviews, difficulty initiating sleep (pre-sleep and bedtime concerns) and emotional concerns affecting sleep reflected as two prominent themes which also emphasised on the importance of including this particular domain.

The "Sleep Quality" domain includes items related to nocturnal awakenings, child's ability to fall back asleep and the need for assistance from caregiver to go back to sleep. This domain also assesses if a poor night's sleep leads to difficulty waking up in the morning and if this is worse on school days when activity demands are higher. Longitudinal analyses have shown poor sleep quality in ADHD cohorts, which is also related to their functional outcomes (Gregory et al 2017; Knight and Dimitriou, 2019).

The "Behaviours in Sleep" domain included items related to parasomnias and physiological sleep problems. Spruyt and Gozal (2011) advocated the need for assessing parasomnias among children with ADHD, as presence of specific parasomnias has been demonstrated in literature (Rodopman-Arman et al 2011). For example, not only do children with ADHD suffer more nightmares (Hvolby et al 2009), the dreams were reported to be more

negative and threatening in nature (Schredell and Sartorius, 2009). Additionally, increased reports of enuresis among this population (O'Brien et al 2003), (supposedly attributed to high arousal threshold) is hypothesized to be due to REM sleep variabilities in this population (Neveus, 2003).

The "Daytime Functions" domain consists of items pertaining to the daytime consequences of the child's poor sleep the previous night as well as effects of excessive daytime sleepiness. Daytime impacts on the child's attention levels, emotional regulation and overall energy were addressed in this domain. Poor sleep has been associated with worse outcomes for both behavioural comorbidities in ADHD children (Lucas et al 2017) as well as poorer neurocognitive outcomes (Sawyer et al 2009). Our qualitative study also highlighted detrimental behavioural and emotional consequences as a result of sleep deprivation.

The "Impact on Family" domain pertains to items describing the detrimental effects of the child's sleep problems on the sleep-wake patterns of their family and household. In addition to more stress being associated with parenting a child with ADHD (Craig et al 2016), presence of sleep problems in the child is related to poorer family outcomes (Sung et al 2008; Lycett et al 16). Prominent impact of child's late sleep onset or disturbed sleep on parent's night schedule or sleep patterns were reported in our qualitative study. Also in our qualitative study, higher scores on child's sleep problem scores were related to more insomnia probability in parents.

The following items wereincluded in 5 domains of the scale, and each can be answered on a 5 point Likert scale, ranging from 'Strongly agree' (5 points); 'Agree'(4 points); No opinion' (3 points); 'Disagree' (2 points) and 'Strongly disagree' (1 points). All items on the five domains of CASS were worded positively so that higher scores indicate increased sleep related problem in that domain. In addition, sleep timing detail questions are included at the end of the scale.

Table 5.1 *Childhood ADHD Sleep Scale (CASS)* Full scale presented in Appendix A.

CASS Domain	Items
Bedtime	1. Child is very active, talkative or busy making plans at bedtime. 2. Child needs consistent routines in the hour before bedtime (eg. snack, bath, reading) 3. Childs can only fall asleep in their carer's bed/not their own bed 4. Child resists going to bed 5. Child struggles to sleep alone, is scared of the dark or needs caregiver in the bedroom to fall asleep 6. Child needs special blankets or other bedclothes to fall sleep. 7. Child is very sensitive to their bedroom's temperature, brightness or noise 8. Child typically takes longer than 30 minutes to fall asleep 9. Child often reports being anxious or worried when trying to fall asleep 10. Child is often upset about not being able to sleep
Sleep Quality	1. Child often awakens during the night 2. Child struggles to fall back asleep if they wake at night 3. Child calls on caregiver to seek reassurance during the night or tries to get into their carers' bed 4. Child often wakes very early in the morning regardless of when they fell asleep the night before 5. Child is often still sleepy for the first hour after wakening 6. Child has significantly worse sleep than other children that I am familiar with 7. Child's sleep is more difficult on school days than on days during the weekend or school holidays 8. On a schoolday morning, the child need an alarm clock or to be woken by someone else.

Behaviours in sleep	1. Child often wets the bed at night. 2. Child often talks during sleep. 3. Child often moves his hands and legs during sleep. 4. Child usually snores, snorts, or gasps during sleep. 5. Child often sleepwalks. 6. Child often has nightmares. 7. Child often grinds his teeth during sleep. 8. Child often awakes screaming and sweating (night terrors)
Daytime Functions	1. Child usually performs their morning routine at a slow pace and seems tired. 2. Child easily loses their temper during morning routine. 3. Child is often sleepy during the day. 4. Child often needs a nap, or falls asleep, during the day. 5. Child is markedly more emotional, difficult, or inattentive after a bad night's sleep
Impacts on family life	1. My own sleep is negatively impacted by my child's sleep problems. 2. The sleep of other household members is negatively impacted by my child's sleep problems. 3. Child's sleep problems negatively impact on my relationships with significant other adults. 4. I am very concerned about my child's sleep.

In addition to the above questions, child's sleep and wake timing questions and perceived effects of medication were also enquired. These questions were treated as descriptive adjuncts to the primary questionnaire and were not added to the scoring of the CASS questionnaire. **Descriptive Adjuncts**	
Medication	1. My child's ADHD medication makes it difficult to fall asleep. 2. My child's ADHD medication makes it difficult for them to sleep through the night without waking. 3. My child's ADHD medication makes it difficult for them to wake up in the morning. 4. If medication for sleep is taken by the child (e.g. melatonin), it helps them fall asleep at night. 5. If medication for sleep is taken by the child (e.g. melatonin), it helps them sleep through the night.
Sleep timing	1. What time does your child go to bed on weekends/holidays 2. What time does your child wake on weekends/holidays 3. What time does your child go to bed on school days/weekdays 4. What time does your child wake on school days/weekdays

Child Sleep Habits Questionnaire (CSHQ):

CSHQ is a 33-item parent report scale to assess the multidimensional sleep problems experienced by the child over the past 30 days (Owens, et al., 2000). Factors of the scale are bedtime resistance, sleep onset-latency, sleep duration, sleep anxiety, night waking, parasomnias, sleep-disordered breathing and daytime sleepiness. Each item is scored on a 3-point scale as occurring "usually" (i.e., 5–7 times within the past week), "sometimes" (i.e., 2–4 times within the past week), or "rarely" (i.e., never or 1 time within the past week). A total CSHQ score of over 41 indicates a paediatric sleep disorder; scores of >41 identify 80% of children with a clinically diagnosed sleep disorder (Owens et al, 2000).

Brown Executive Functions and Attention scales (Brown- EFA)

The Brown Executive Function/Attention Scales (Brown EF/A Scales) provide an easily understandable, standardized tool to collect information about the problems an individual demonstrates or reports with executive functions, the self-management functions that support attention in multiple tasks of daily life (Brown, 2005). Results are compared with norms to indicate how any reported problems over the past 6 months (or since the assessment was last administered) compared to other people of similar age. Raw scores and standard scores for the total score and the 6 domains (activation, focus, effort, emotion, memory, and action) are generated. For this study the parent rating version for 8-12 year and 3–7-year-old children was used.

Data Analysis

After screening and cleaning, scores from each scale were computed and the required total and sub-factor scores were collated in SPSS 28.0 (IBM Corporation). Three separate SPSS data files were created: the first file included all participant's demographic characteristics, computed scores for CSHQ, Brown EFA scale, the original unreduced CASS scores (for both

test-retest data) and the reduced CASS scores. The second and third SPSS data file consisted of each participant's individual item scores on the original unreduced CASS (for test and re-test data respectively). Descriptive statistical analysis was completed for the data to generate means, standard deviations, percentage frequencies, and composite scores was assessed for normality and presence of outliers using the Shapiro Wilk test and examination of histograms. CASS scores for both time 1 and time 2 were separately documented for the ADHD and the control group. Legitimate values were noted as outliers through Box blots. Distributions of the CASS scores and tests of normality were performed. Spearman's rank order correlation coefficient was used to determine the relationship among the CASS domains, and between the CASS domains and CSHQ and Brown EFA domains for the ADHD and the control group. Nonparametric Mann Whitney U tests were used to assess group differences between ADHD and control group for the CASS, CSHQ and Brown EFA as the scores were not normally distributed. $P<0.05$ was interpreted as indicating statistically significant differences and associations, and effect sizes were interpreted according to Cohen (1988).

Test-retest reliability of the CASS was estimated by computing the correlation coefficient of the measured CASS scores at time 1 (1^{st} administration) and time 2 (after 2 weeks). Internal consistency of the CASS scale was measured by computing the Cronbach's alpha for the total score and the domain scores. Cronbach alpha values of 0.7 and above are considered acceptable and above 0.9 is considered excellent.

The Kaiser-Meyer-Olkin Measure of Sampling Adequacy and Bartlett's Test of Sphericity were used to assess the suitability of the data for conducting Exploratory Factor Analysis (EFA). EFA was first performed using Principal Axes Factoring with varimax rotation and eigenvalues > 1. Additionally, we performed EFA with varimax rotation and imposing a four-factor solution to explore the theoretical structure of the CASS. Resultant reduced CASS

was then subjected to preliminary descriptive analysis, reliability analysis and correlation with the CSHQ scale and Brown EFA scales.

5.3 Results

Descriptive statistics

Table 5.2 presents the demographic information for the children and parent's age, their gender, children with an ADHD diagnosis and their use of medication, and the parent reported sleep and wake time of the children. A total of 107 parents (87.6 % mothers) between the age of 32 and 57 years (average age- 42.35 years) completed the questionnaires for their children (69.2 % males). Out of the 107 children reported for, 59 (55.1%) had received a diagnosis of ADHD and 36.2% of those diagnosed were on prescribed medication targeting the core and associated symptoms.

Table 5.2 *Demographic characteristics of study participants*

Variables	Child	Parent
Age (years), Mean (SD) (range)	n = 107 8.84 (2) (5-12)	n = 107 42.35 (4.81) (32-57)
Gender, N (%)	n = 107 Male= 74 (69.2%) Female=33(30.8%)	n = 105 Male= 13 (12.4%) Female= 92 (87.6%)
ADHD diagnosis, N (%)	59 (55.1%)	
Medication, N (%)	21 (36.2%)	
School day sleep onset time (hh:mm PM), Mean (SD) (range)	n = 107 21:35 (1:03) (18:30 – 00:30)	
School day wake time (hh:mm AM), Mean (SD) (range)	n = 107 7:08 (0:41) (5:00- 8:45)	
Holiday sleep onset time (hh:mm PM), Mean, (SD) (range)	n = 107 22:01 (1:14) (18:30 – 01:00)	
Holiday wake time (hh:mm AM), Mean, (SD) (range)	n = 107 7:57 (1:17) (4:30 – 12:00)	

Note: SD – Standard Deviation, % - Percentage, N = Frequency

Sleep and wake timing on school days and holidays did not differ by gender, however school day sleep and wake time and holiday sleep time differs among the ADHD and non-ADHD groups (ADHD, n=59, median school sleep = 22:00 (IQR= 1:30) vs. Non-ADHD, n=48, median school sleep = 21:00 (IQR=1:00), U = 1020.5, P< 0.05, r= 0.23, small effect size; ADHD, n=59, median school wake = 7:00 (IQR= 1:00) vs. Non-ADHD, n=48, median school wake = 7:22 (IQR= 0:30), U = 1024, P< 0.05, r= 0.23, small effect size; ADHD, n=59, median holiday sleep = 22:00 (IQR=1:30) vs. Non-ADHD, n=48, median holiday wake = 21:30 (IQR=1:41), U = 1024, P< 0.05, r= 0.23, small effect size (Table 5.3).

Table 5.3 *Sleep and wake times across ADHD and Non-ADHD group*

Variable	ADHD n= 59	Non-ADHD n= 48	Mann Whitney U, (Z Statistic), (effect size)
School day sleep onset time (hh:mm, PM), Mean (SD)	21:49 (1:05) (19:30 – 00:30)	21:18 (0:56) (18:30 – 23:00)	1020.5*(-2.48), (0.23)
School day wake time, Mean (SD)	6:58 (0:46) (5:00- 8:45)	7:20 (0:29) (5:45- 8:30)	1024*(-2.48), (0.23)
Holiday sleep onset time (hh:mm, PM), Mean, (SD)	22:18 (1:16) (20:00 – 01:00)	21:42 (1:06) (18:30 – 24:00)	1024*(-2.46), (0.23)
Holiday wake time, Mean, (SD)	7:54 (1:34) (4:30 – 12:00)	8:01 (0:50) (5:45 – 10:00)	1215.5 (-1.26)

Note. * = p < .05.

Table 5.4 shows the descriptive statistics for Time 1 (n = 107) and Time 2 (n = 70) CASS scores. All scores on Time 1 CASS differed among the ADHD and Non-ADHD groups.Whereas, for Time 2, all but Daytime Function scores do not differ among the groups (P = 0.074). Figure 5.1 demonstrates violin plots presenting the distribution of CASS domain scores (time 1) among ADHD and non-ADHD groups.

Table 5.4 *CASS scores for Time 1 and 2 across ADHD and non- ADHD scores*.

	Domain Scores	**ADHD** N= 59 M (SD), Min-Max	**Non-ADHD** N= 48 M (SD), Min-Max	**Mann Whitney U, (Z Statistic), (effect size)**
Time 1 (N=107)	CASS total score	117.05 (21.18), 58-150	91.42 (28.82), 45-154	678*** (-4.62), (0.4)
	Bedtime	37.59 (7.05), 17-48	28.58 (10.10), 13-49	679*** (-4.62), (0.4)
	Sleep Quality	28.02 (6.61), 11-44	21.94 (7.28), 8-36	770*** (-4.05), (0.3)
	Behaviours in sleep	20.98 (5.93), 8-35	17.13 (6.70), 8-34	901** (-3.23), (0.3)
	Daytime Functions	16.37 (3.82), 6-23	14.19 (4.11), 5-25	955** (-2.90), (0.2)
	Impacts on family	14.02 (4.59), 4-20	9.58 (5.65), 4-20	791*** (-3.92), (0.3)
		N= 44	N= 26	
Time 2 (N=70)	CASS total score	118.20 (20.32), 80-154	91.12 (29.59), 47-153	278*** (-3.57), (0.4)
	Bedtime	37.61 (6.39), 22-49	28.73 (10.67), 14-46	295*** (-3.37), (0.4)
	Sleep Quality	28.59 (5.88), 16-38	21.08 (7.52), 8-39	245*** (-3.97), (0.4)
	Behaviours in sleep	21.66 (6.33), 8-34	17. 27 (6.47), 9-33	325** (-3.01), (0.36)
	Daytime Functions	16.27 (4.05), 5-23	14.15 (5.11), 5-25	426 (-1.78),
	Impacts on family	14.07 (4.59), 4-20	9.88 (5.30), 4-20	312** (-3.16), (0.3)

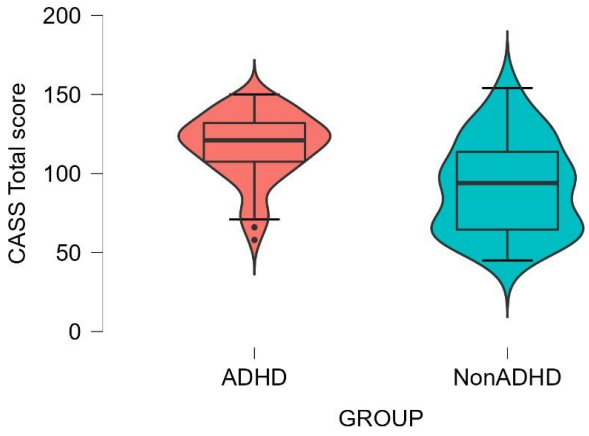
Note- M=Mean, SD=Standard Deviation, ** = p < .01, *** = p < .001

Table 5.5 shows medication status for the ADHD group at Time 1 and Time 2 of CASS administration.

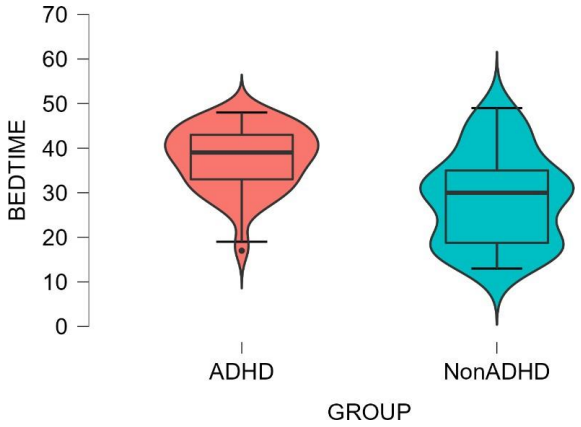
Table 5.5 *ADHD and sleep medication*

Domain Scores	Time 1	Time 2
ADHD medication, N (%)	17 (28.8%)	13 (29.5%)
Sleep medication N (%)	14 (23.7%)	10 (22.7%)

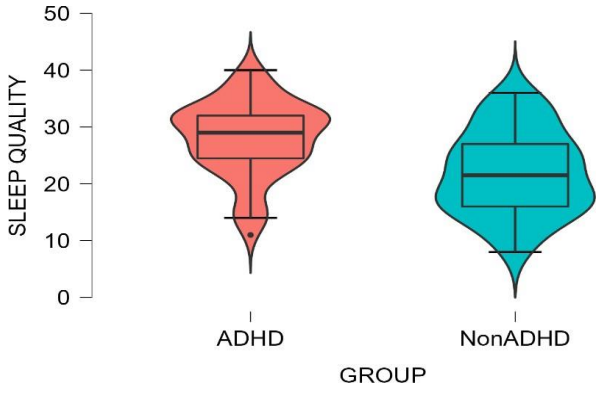
A. CASS Total score across ADHD and non-ADHD groups



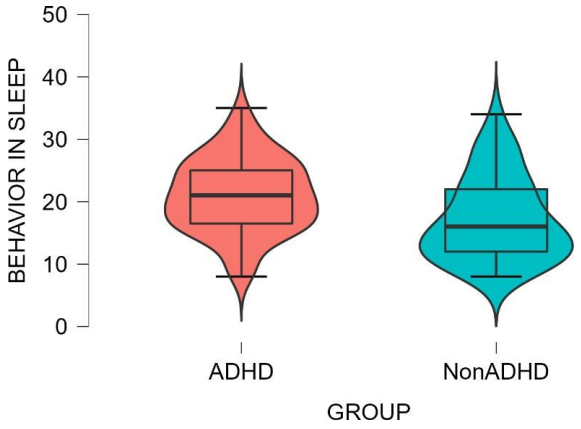
B. Bedtime score across ADHD and non-ADHD groups



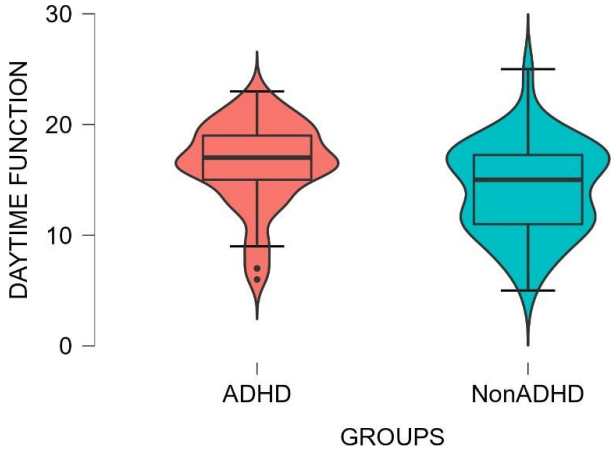
C. Sleep Quality across ADHD and non-ADHD groups



D. Behaviours in Sleep across ADHD and non-ADHD groups



E. Daytime Functions across ADHD and non-ADHD groups



F. Impacts on Family score across ADHD and non-ADHD groups.

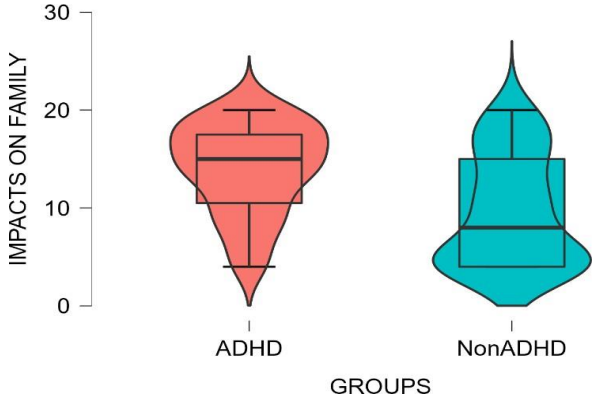


Figure 5.1 *Violin element Box plots for CASS Domains (Time 1 scores) across the ADHD and non-ADHD groups. All scores differences between ADHD and Non-ADHD groups are statistically significant at p < .01 and p < .001.*

CASS total score (time 1) and the scores on its five domains did not differ based on medication status for the ADHD group (Table 5.6).

Table 5.6 *CASS score differences among the medicated and unmedicated ADHD group.*

Domain Scores	**MEDICATION** N= 21 M (SD), Min-Max	**NO MEDICATION** N= 37 M (SD), Min-Max	**Mann Whitney U, (Z Statistic), (effect size)**
CASS total score	114.52 (21.64), 71-144	118.32 (21.35), 58-150	353 (-0.57)
Bedtime	36.62 (5.92), 26-47	37.92 (7.62), 17-48	315 (-1.19)
Sleep Quality	28.52 (6.53), 14-38	27.70 (6.81), 11-40	355.5 (-0.535)
Behaviours in sleep	19.71 (6.26), 8-32	21.86 (5.67), 9-35	298.5 (-1.45)
Daytime Functions	15.76 (4.58), 6-22	16.70 (3.40), 7-23	367.5 (-0.342)
Impacts on family	13.90 (4.72), 4-20	14.03 (4.63), 4-20	380 (-0.130

Note- M=Mean, SD=Standard Deviation.

Table 5.7 shows CASS (time 1) score differences across genders.

Table 5.7. *CASS score differences across genders.*

Domain Scores	**Male** N= 74, M (SD), Min-Max	**Female** N= 33, M (SD), Min-Max	**Mann Whitney U, (Z Statistic)**
CASS total score	105.69 (27.54), 52-154	105.24 (29.03), 45-150	1216 (-0.034)
Bedtime	33.51 (9.49), 14-48	33.64 (10.07), 13-49	1212 (-0.061)
Sleep Quality	25.51 (7.60), 9-40	24.79 (7.44), 8-30	1108 (-0.760)
Behaviours in sleep	19.35 (6.52), 8-34	19.03 (6.71), 8-35	1185 (-0.240)
Daytime Functions	15.19 (4.12), 6-25	15.85 (4.04), 5-22	1075 (-0.989)
Impacts on family	12.12 (5.48), 4-20	11.82 (5.72), 4-20	1188 (-0.220)

Note- M=Mean, SD=Standard Deviation

	Domain Scores	**Male,** N= 74 M (SD), Min-Max	**Female,** N= 33 M (SD), Min-Max	**Mann Whitney U, (Z Statistic), (effect size)**
CSHQ (N=105)	CSHQ total score	50.58 (12.37), 31-79	49.64 (10.93), 32-72	1150(-0.262)
	Bedtime Resistance	9.90 (3.58), 5-16	9.48 (3.69), 6-18	1111 (-0.533)
	Sleep onset delay	2.15 (0.88), 1-3	2.12 (0.78), 1-3	1148 (-0.292)
	Sleep Duration	4.92 (1.92), 3-9	5.15 (1.85), 3-9	1087 (-0.717)
	Sleep Anxiety	7.17 (2.87), 4-12	7.12 (2.88), 4-12	1170 (-0.123)
	Night Waking	5.18 (2.02), 3-9	4.33 (1.31), 3-7	937 (-1.77)
	Parasomnias	9.89 (2.45), 7-16	9.67 (2.23), 7-15	1144 (-0.30)
	Sleep Disordered Breathing	3.75 (1.30), 3-9	3.61 (1.34) 3-8	1185 (-0.874)
	Daytime sleepiness	11.31 (4.21), 6-19	11.06 (3.85), 6-19	1182 (-0.042)
Brown EFA (N=106)	Brown EFA total	100.9 (46.24), 0-165	80.18 (53.35) 3-158	946 (-1.76)
	Activation	16.56 (8.05), 0-26	12.18 (8.04) 0-26	839* (-2.49), (0.24)
	Focus	17.92 (8.84) 0-30	13.91 (10.44) 0-30	961 (-1.66)
	Effort	16.64 (7.94), 0-27	13.21 (8.91), 0-27	943 (-1.78)
	Emotion	15.55 (7.61), 0-27	13.21 (8.06), 0-26	1013 (-1.30)
	Memory	14.79 (8.38), 0-29	11.70 (9.59), 0-27	1002 (-1.38)
	Action	19.44 (8.53), 0-30	15.97 (10.21), 0-30	985 (-1.49)

Table 5.8 *CSHQ and Brown EFA scores across genders.* Note- M=Mean, SD=Standard Deviation, * = $p < .05$.

Scores for CASS or CSHQ did not differ by gender (Table 5.7 and Table 5.8 respectively) , however a Mann Whitney U-Test revealed that Brown EFA differed by gender

only for the activation domain (male, n=73, median Activation =18 (IQR=10) vs. female, n=33, median Activation= 13 (IQR=15), U = 839.5, P< 0.05, r= 0.24 (small effect size)) (Table 5.8).

Table 5.9: *CSHQ and Brown EFA scores among ADHD and Non-ADHD groups*

	Domain Scores	**ADHD** N= 57 M (SD), Min-Max	**Non-ADHD** N= 48 M (SD), Min-Max	**Mann Whitney U, (Z Statistic), (effect size)**
CSHQ (N=105)	CSHQ total score	54.19 (10.46), 34-79	45.65 (11.92), 31-75	787*** (-3.73), (0.3)
	Bedtime Resistance	10.46 (3.32), 6-16	8.96 (3.79), 5-18	953** (-2.69), (0.2)
	Sleep onset delay	2.39 (0.77), 1-3	1.85 (0.85), 1-3	906** (-3.18), (0.3)
	Sleep Duration	5.47 (1.9), 3-9	4.42 (1.74), 3-9	930** (-2.89), (0.2)
	Sleep Anxiety	7.86 (2.86), 4-12	6.31 (2.64), 4-12	933** (-2.84), (0.2)
	Night Waking	5.39 (1.83), 3-9	4.35 (1.76), 3-9	886** (-3.17), (0.3)
	Parasomnias	10.51 (2.43), 7-16	9 (2.04), 7-14	843*** (-3.41), (0.3)
	Sleep Disordered Breathing	3.89 (1.46), 3-9	3.48 (1.09) 3-8	1130 (-1.88)
	Daytime sleepiness	11.74 (4.26), 6-19 N=58	10.63 (3.83), 6-19 N=48	1156 (-1.36)
Brown EFA (N=106)	Brown EFA total	123.17 (21.94), 71-165	59.75 (50.98) 0-164	490** (-5.72), (0.5)
	Activation	19.79 (4.03), 9-26	9.65 (8.68) 0-26	519*** (-5.55), (0.5)
	Focus	21.95 (5.42) 8-30	10.29 (9.50) 0-29	489*** (-5.73), (0.5)
	Effort	20.22 (3.75), 11-27	9.96 (8.97), 0-27	546*** (-5.38), (0.5)
	Emotion	19.02 (4.62), 5-27	9.75 (7.87), 0-26	490*** (-5.73), (0.5)
	Memory	18.69 (5.59), 5-28	7.96 (8.52), 0-29	461*** (-5.91), (0.5)
	Action	23.5 (4.63), 10-30	12.15 (9.5), 0-30	495*** (-5.69), (0.5)

Note- M=Mean, SD=Standard Deviation, ** = $p < .01$, *** = $p < .001$

For CSHQ scores, all but sleep disordered breathing and Daytime sleepiness did not differ between ADHD and Non-ADHD groups (P = 0.06 and P = 0.17, respectively) (Table 5.9). All domains of Brown EFA scores differed significantly across ADHD and Non-ADHD groups (Table 5.9). Figure 5.2 shows raincloud plots demonstrating differences in CASS, CSHQ and Brown EFA scores across ADHD and non-ADHD groups, while figure 5.3 shows the raincloud plots for the CASS (time 1) domain scores across ADHD and non-ADHD groups.

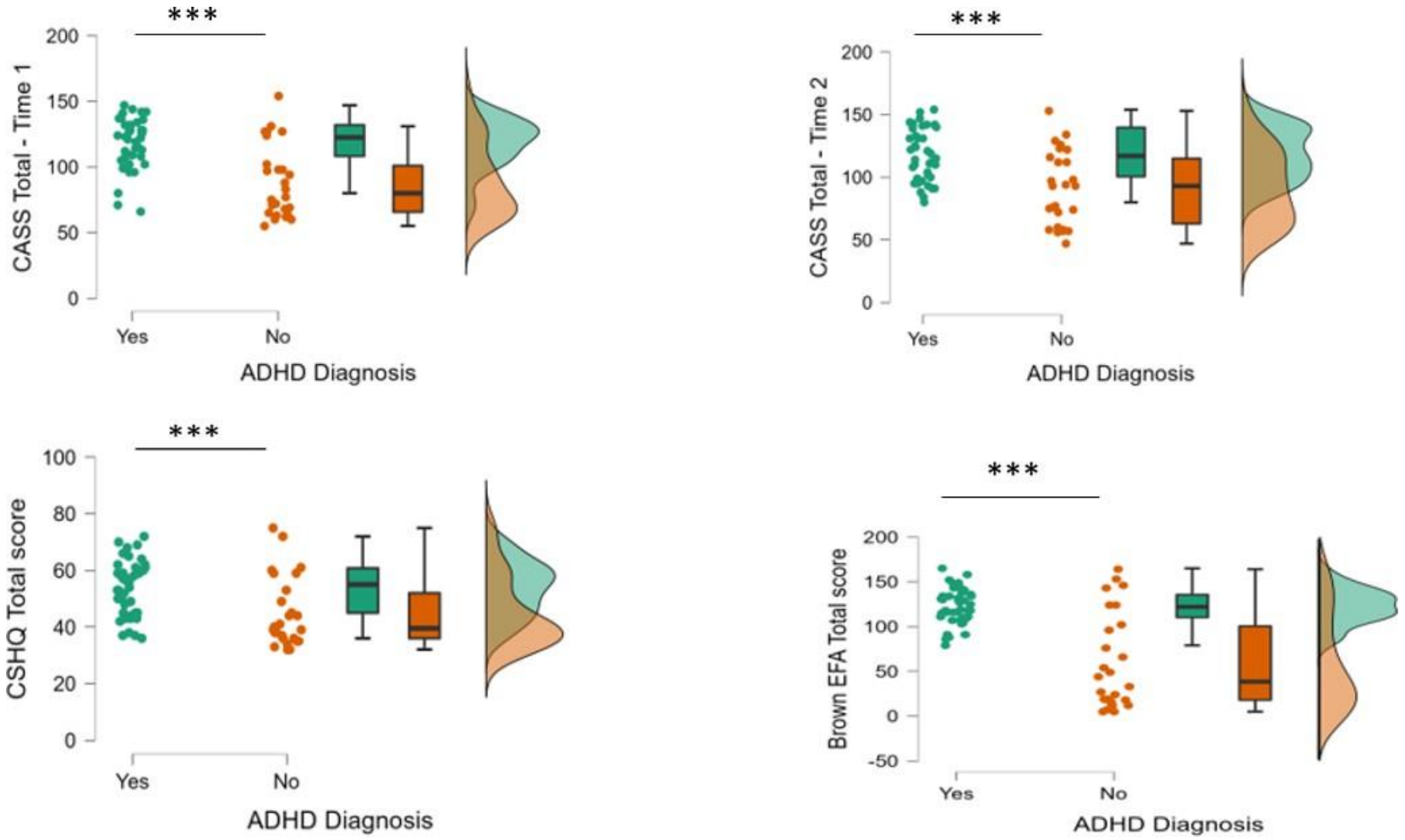


Figure 5.2 *Raincloud Plots showing difference in CASS (Time 1 and 2), CSHQ and Brown EFA scores among the ADHD and non-ADHD groups.*

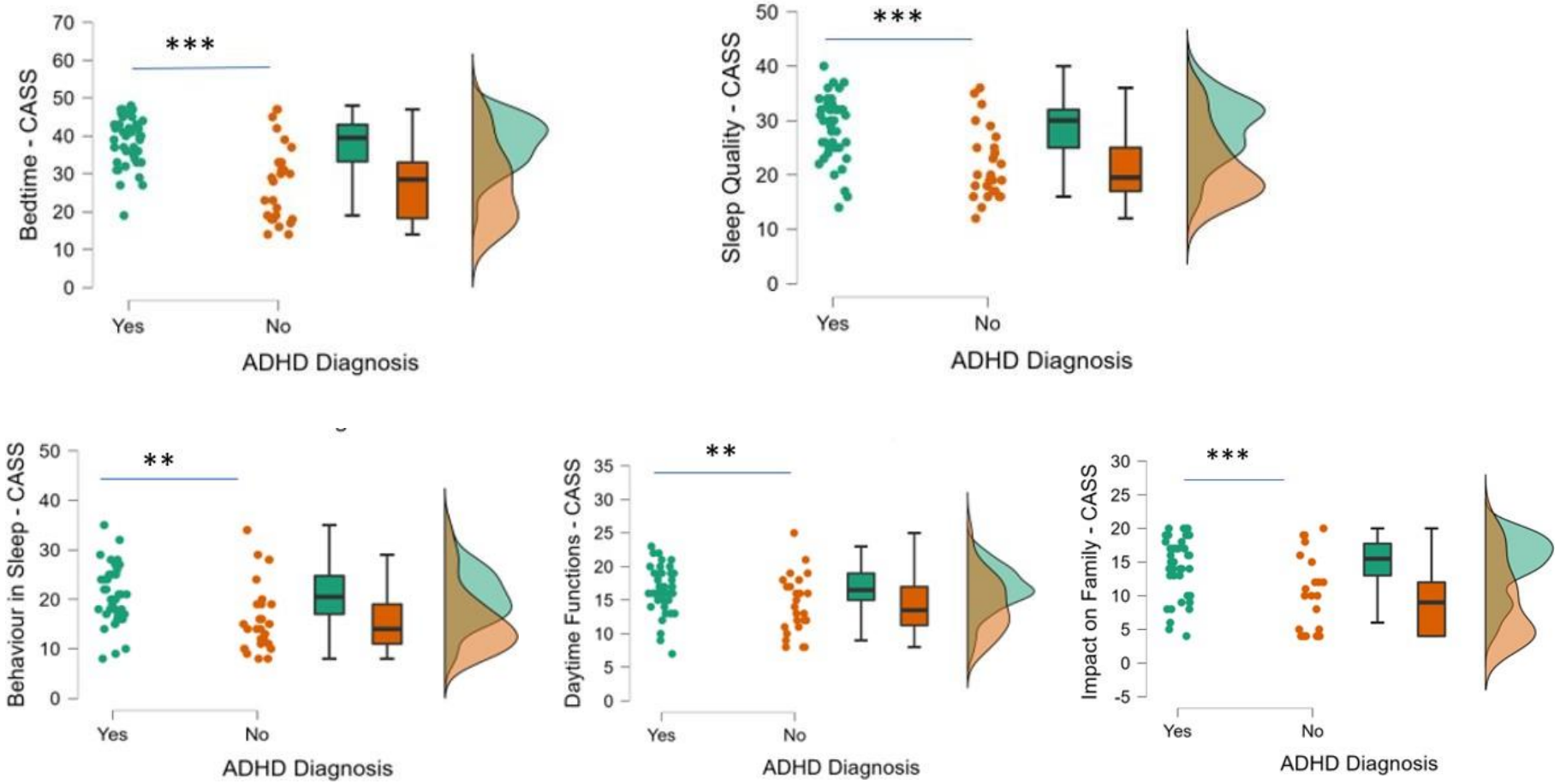


Figure 5.3 *Raincloud Plots showing difference in CASS (time 1) domains among the ADHD and non-ADHD groups.*

Cross-Correlations between CASS Domains

Table 5.10, 5.11 and 5.12 show the correlations between the CASS (Time 1) scores. All CASS domains were found to be significantly associated at $P < 0.01$ level for the combined sample and the non-ADHD group. However, within the ADHD group, no association was found for Daytime Functions with Behaviours in Sleep or Impacts on Family domains ($P = 0.373$ and $P = 0.114$, respectively) (Table 5.11).

Table 5.10. *Correlation between CASS domain scores (Time 1) combined group (N=107). Spearman's rho and confidence intervals have been presented.*

Domain	Bedtime	Sleep Quality	Behaviour in Sleep	Daytime Function
Sleep Quality	0.728** (0.622, 0.809)			
Behaviour in sleep	0.481** (0.315, 0.618)	0.603** (0.462, 0.714)		
Daytime Function	0.545** (0.391,0.669)	0.585** (0.440, 0.700)	0.406** (0.228, 0.557)	
Impacts on Family	0.702** (0.587, 0.789)	0.766** (0.671, 0.836)	0.552** (0.400, 0.675)	0.472** (0.305, 0.611)

Note- ** = p < .01 level.

Table 5.11 *Correlation between CASS domain scores (Time 1) ADHD group (N=59). Spearman's rho and confidence intervals have been presented.*

Domain	Bedtime	Sleep Quality	Behaviour in Sleep	Daytime Function
Sleep Quality	0.540** (0.323, 0.704)			
Behaviour in sleep	0.237 (-0.028, 0.471)	0.479** (0.247, 0.659)		
Daytime Function	0.306* (0.046,0.527)	0.435** (0.193, 0.626)	0.118 (-0.150, 0.370)	
Impacts on Family	0.449** (0.211, 0.637)	0.656** (0.474, 0.784)	0.415** (0.171, 0.612)	0.208 (-0.059, 0.447)

Note- ** = p < .01 level, * = p < .05 level.

Table 5.12 *Correlation between CASS domain scores (Time 1) Non-ADHD group (N=48). Spearman's rho and confidence intervals have been presented.*

Domain	Bedtime	Sleep Quality	Behaviour in Sleep	Daytime Function
Sleep Quality	0.765** (0.608, 0.864)			
Behaviour in sleep	0.553** (0.311, 0.727)	0.562** (0.323, 0.733)		
Daytime Function	0.675** (0.477,0.808)	0.652** (0.445, 0.793)	0.517** (0.265, 0.703)	
Impacts on Family	0.808** (0.675, 0.890)	0.788** (0.644, 0.878)	0.520** (0.268, 0.705)	0.649** (0.441, 0.791)

Note- ** = $p < .01$ level.

Reliability Analysis for the CASS

Reliability analysis was performed on the novel CASS scale which consisted of 35 items. Cronbach's Alpha for the tool was computed to be $\alpha = 0.910$ indicating excellent reliability. Table 5.13 shows Cronbach's Alpha values for each CASS domains among the combined sample, ADHD and non-ADHD groups. Results demonstrate values ranging above 0.6 for all domains.

Table 5.13 *Cronbach's Alpha of CASS scale domains for combined ADHD and Non-ADHD groups.*

Scale (n items)	COMBINED N= 106	ADHD N= 58	NON-ADHD N=48
Bedtime (10)	0.703	0.744	0.639
Sleep Quality (8)	0.739	0.603	0.785
Behaviours in sleep (8)	0.760	0.667	0.808
Daytime Functions (5)	0.681	0.654	0.694
Impacts on Family (4)	0.914	0.865	0.923

Table 5.14 presents the test-retest reliability for CASS scores between Time 1 and Time 2 for parents of children with or without ADHD and the combined sample results. Figure 5.4 presents the correlation between CASS total scores for time 1 and time 2.

Table 5.14. *Test-retest reliability correlation coefficient between Time 1 and Time 2 CASS scores for parents of children with or without ADHD. Spearman's rho values and confidence intervals have been presented. (ADHD Time 1 n= 59, ADHD Time 2 n= 44, Non ADHD Time 1 n= 48, Non ADHD Time 2 n= 26)*

CASS domains	COMBINED	ADHD	NON-ADHD
CASS total	0.817*** (0.718, 0.884)	0 .739*** (0.559, 0.892)	0.820*** (0.627, 0.918)
Bedtime	0.813*** (0.711, 0.882)	0.697*** (0.498, 0.827)	0.816*** (0.619, 0.916)
Sleep quality	0.766*** (0.643, 0.850)	0.631*** (0.404, 0.785)	0.834*** (0.652, 0.925)
Behaviour in sleep	0.862*** (0.783,0.913)	0.784*** (0.629, 0.879)	0.861*** (0.705, 0.938)
Daytime functions	0.622*** (0.448, 0.751)	0.561*** (0.309, 0.740)	0.601*** (0.267, 0.806)
Impact on Family	0.849*** (0.764, 0.905)	0.761*** (0.594, 0.865)	0.877*** (0.736, 0.945)

Note- *** = p < .001 level

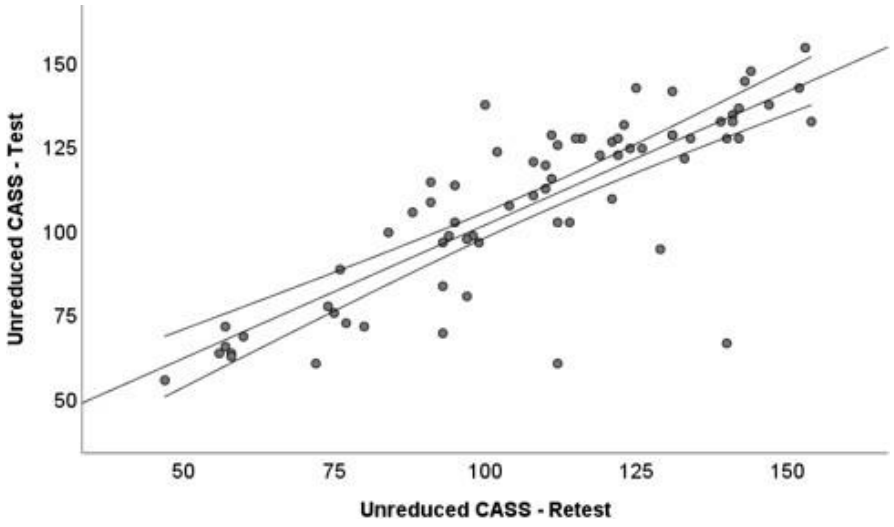


Figure 5.4 *Scatterplot showing the correlation between Time 1 and Time 2 CASS total scores.*

A two-way repeated measures ANOVA was performed to determine whether any change in CASS total score is the result of the interaction between ADHD diagnosis category and time. There was a statistically significant effect of ADHD diagnosis on CASS total scores ($F(1,68) = 28.01$, $p = < 0.001$), however no interaction effect of ADHD diagnosis and time ($p = 0.47$) or no main effect of time was present ($p = 0.68$). Figure 5.5 shows the above significant effect.

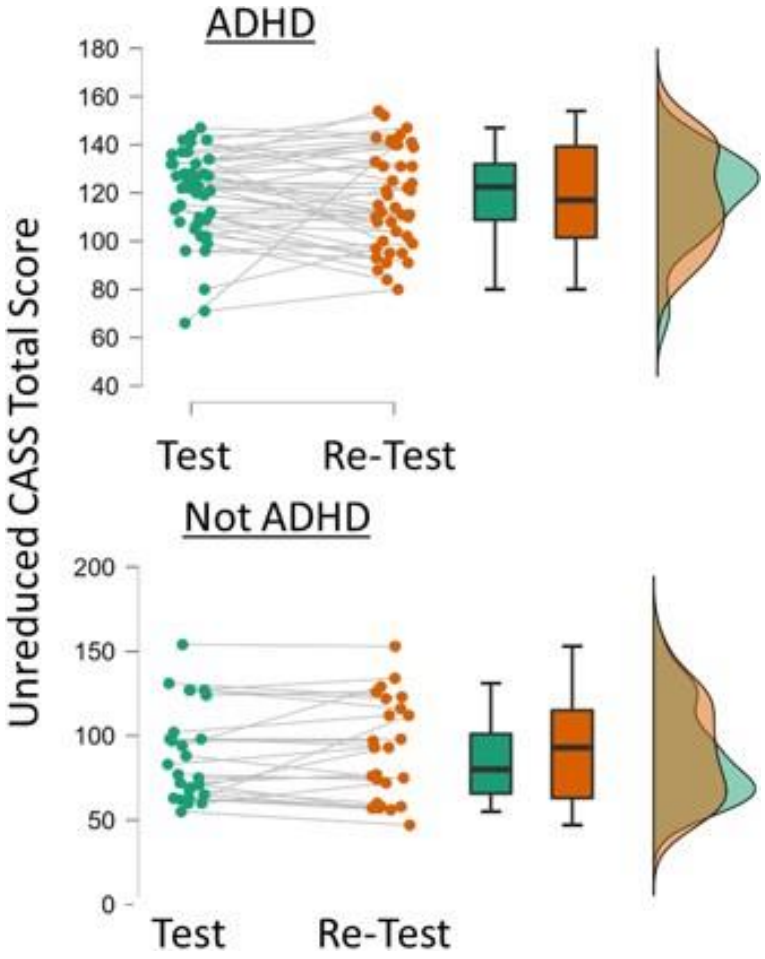


Figure 5.5 *Effect of ADHD diagnosis on CASS total scores across Time 1 and Time*

Exploratory Factor Analysis (EFA) of the CASS

We performed EFA on the CASS to explore dimensionality of the 35 original items, to undertake informed item reduction and to ensure that the self-developed items are valid and

reliable to assess sleep in childhood ADHD. The Principal Axes Factoring method with Varimax rotation was used to produce the EFA models for CASS. Coefficients below 0.04 were supressed. Table 5.15 shows the pattern matrix of the factors for the final model for corrected item correlations, after illegitimate item were removed. Items having multiple factor loadings (above the designated coefficient value), negative loadings, items with no factor loadings and small single loadings were removed. The final 4 factor model for CASS was a result of 5 EFAs. Criteria for KMO test of sample adequacy and Bartlett test of Sphericity were met for each EFA.

The last column of Table 5.15 presents the item communalities which is the proportion of each item's variance that can be explained by the derived factors. The item, 'child often has nightmares' had 94.7 % variance explained by the derived factors, while two items in particular ('child is very active, talkative or busy making plans at bedtime', and 'child can only fall asleep in their carer's bed') have only 28.9% and 28.2% variance explained by the derived factors.

The analysis yielded four factors explaining a total of 54.52 % of the variance for the entire set of items. Factor 1 was labelled "Sleep problems and Impacts", which explained 34.84% of the variance; factor 2 was labelled "Executive and Sensory Regulation", which explained 8.35% of the variance; factor 3 was labelled "Daytime Functions", which explained 6.13% of the variance, and factor 4 was labelled "Parasomnias", which explained 5.18% of the variance. Table 5.16 shows the reduced CASS derived from the original CASS scale.

Table 5.15 *Exploratory Factor Analysis of CASS: Pattern Matrix of Final Model*

	CASS Items	Loadings				Communality
		Factor 1 – Sleep problems and impacts	Factor 2 – Executive and sensory regulation	Factor 3 – Daytime functions	Factor 4 - Parasomnias	
1	Child often awakens during the night	**0.543**	0.137	-0.085	0.278	0.399
2	Child struggles to fall back asleep if they wake at night	**0.657**	0.188	0.025	0.207	0.511
3	Child has significantly worse sleep than other children that I am familiar with	**0.713**	0.339	0.203	0.085	0.671
4	My own sleep is negatively impacted by my child's sleep problems	**0.808**	0.234	0.175	0.108	0.750
5	The sleep of other household members is negatively impacted by my child's sleep problems	**0.749**	0,245	0.074	0.131	0.644
6	Child's sleep problems negatively impact on my relationships with significant other adults in the household	**0.838**	0.189	0.150	0.148	0.782
7	I am very concerned about my child's sleep	**0.728**	0.350	0.332	0.107	0.774
8	Child is very active, talkative, or busy making plans at bedtime.	0.238	**0.460**	-0.045	0.136	0.289
9	Child needs consistent routines in the hour before bedtime (e.g. snack, bath, reading)	0.124	**0.521**	0.021	0.178	0.319
10	Childs can only fall asleep in their carer's bed/not their own bed	0.197	**0.478**	0.114	0.046	0.282
11	Child needs special blankets or other bedclothes to fall sleep.	0.161	**0.612**	0.215	-0.033	0.448
12	Child is very sensitive to their bedroom's temperature, brightness, or noise	0.328	**0.642**	0.199	0.178	0.591
13	Child is markedly more emotional, difficult, or inattentive after a bad night's sleep	0.148	**0.544**	0.244	0.103	0.388
14	Child is often still sleepy for the first hour after wakening	0.127	0.082	**0.803**	-0.010	0.668
15	On a school day morning, the child needs an alarm clock or to be woken by someone else	-0.002	0.173	**0.566**	0.090	0.358
16	Child usually performs their morning routine at a slow pace and seems tired	0.227	0.164	**0.799**	0.079	0.723
17	Child often talks during sleep	0.276	0.270	-0.019	**0.451**	0.353
18	Child often has nightmares	0.278	0.035	0.166	**0.917**	**0.947**
19	Child often awakes screaming and sweating (night terrors)	0.102	0.162	0.059	**0.651**	0.464
	Eigenvalue	7.008	2.019	1.530	1.464	
	% Of total variance	36.88%	10.62 %	8.05%	7.70%	

Table 5.16 *Reduced CASS derived from original CASS items*

FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4
Sleep Quality item 1: Child often awakens during the night	Bedtime item 1: Child is very active, talkative, or busy making plans at bedtime.	Sleep quality item 5: Child is often still sleepy for the first hour after wakening	Behaviours in sleep item 2: Child often talks during sleep
Sleep Quality item 2: Child struggles to fall back asleep if they wake at night.	Bedtime item 2: Child needs consistent routines in the hour before bedtime (e.g. snack, bath, reading)	Sleep Quality item 8: On a school day morning, the child needs an alarm clock or to be woken by someone else	Behaviours in sleep item 6: Child often has nightmares
Sleep Quality item 6: Child has significantly worse sleep than other children that I am familiar with	Bedtime item 3: Childs can only fall asleep in their carer's bed/not their own bed	Daytime functions item 1: Child usually performs their morning routine at a slow pace and seems tired	Behaviours in sleep item 8: Child often awakes screaming and sweating (night terrors)
Impact on family and household item 1: My own sleep is negatively impacted by my child's sleep problems	Bedtime item 6: Child needs special blankets or other bedclothes to fall sleep.		
Impact on family and household item 2: The sleep of other household members is negatively impacted by my child's sleep problems	Bedtime item 7: Child is very sensitive to their bedroom's temperature, brightness, or noise		
Impact on family and household item 3: Child's sleep problems negatively impact on my relationships with significant other adults in the household	Daytime functions item 5: Child is markedly more emotional, difficult, or inattentive after a bad night's sleep		
Impact on family and household item 4: I am very concerned about my child's sleep			
Sleep Problems and Impacts	Executive And Sensory Regulation	Daytime Functions	Parasomnias

Exploring the Reduced CASS Scale

Table 5.17 shows the Reduced CASS scores across the participant groups. All scores differ among the ADHD and the Non-ADHD groups, except for Daytime functions (P = 0.21).

Table 5.17 *Reduced CASS score differences among ADHD and Non-ADHD group.*

Scores	**ADHD** N= 58 M (SD), Min-Max	**Non-ADHD** N= 48 M (SD), Min-Max	**Mann Whitney U, (Z Statistic), (effect size)**
Reduced CASS total	65.28 (12.8), 30-87	51.79 (16.63), 25-84	765*** (-3.97), (0.3)
Sleep problems and impacts	24.34 (7.42), 7-35	16.54 (8.38), 7-32	688*** (-4.47), (0.4)
Executive and sensory regulation	22.72 (4.36), 10-29	18.81 (5.69), 6-30	835*** (-3.54), (0.3)
Daytime functions	10.71 (3.85), 3-15	10 (3.48), 3-15	1199 (-1.23)
Parasomnias	7.50 (2.99), 3-15	6.44 (3.43), 3-15	1069* (-2.05), (0.2)

Note- *** = p < .001 level, * = p < .05 level.

Table 5.18 shows the reduced CASS scores among ADHD group who were on and not on medication: reduced CASS total score (P = 0.95) and scores for Sleep Problems and Impacts; Executive and Sensory regulation; Daytime Functions; and Parasomnias), did not differ among the medicated and un-medicated groups (P = 0.79, P = 0.76, P = 0.98, P = 0.09, respectively).

Table 5.18 *Reduced CASS score differences among the medicated and unmedicated ADHD group.*

Scores	**MEDICATION** N= 21 M (SD), Min-Max	**NO MEDICATION** N= 37 M (SD), Min-Max	**Mann Whitney U, (Z Statistic), (effect size)**
Reduced CASS total score	64.90 (14.18), 37-86	65.35 (12.35), 30-87	366.5 (-0.059)
Sleep problems and impacts	24.65 (7.70),	24.16 (7.46),	354.5 (-0.260)
Executive and sensory regulation	23.15 (3.37), 18-29	22.35 (4.80), 10-28	325.5 (-0.294)
Daytime functions	10.50 (4.44), 3-15	10.76 (3.60), 3-15	369 (-0.017)
Parasomnias	6.60 (2.78), 3-11	8.08 (3), 3-15	272 (-1.648)

Note- M=Mean, SD=Standard Deviation

Cross-correlation between Reduced CASS domains:

Cross correlations between the reduced CASS factors were found for the combined group and the non-ADHD group (tables 5.19 and 5.21 respectively). However, for ADHD group (Table 5.20) correlations were found only between Parasomnias and Sleep problems and impacts (rho = 0.45, P <0.001); and between Daytime functions and Executive and sensory regulation (rho = 0.27, P <0.05).

Table 5.19 *Correlation between REDUCED CASS factor scores combined group (N=106). Spearman's rho and confidence intervals have been presented.*

Domain	Sleep problems and impacts	Executive and sensory regulation	Daytime functions
Executive and sensory regulation	0.506*** (0.344, 0.639)		
Daytime functions	0..310*** (0.121, 0.477)	0.318*** (0.130, 0.484)	

Parasomnias	0.509*** (0.347,0.641)	0.348*** (0.163, 0.510)	0.245* (0.052, 0.421)

Note- *** = p < .001 level, * = p < .05 level.

Table 5.20 *Correlation between REDUCED CASS factor scores ADHD group (N=58). Spearman's rho and confidence intervals have been presented.*

Domain	Sleep problems and impacts	Executive and sensory regulation	Daytime functions
Executive and sensory regulation	0.187 (-0.82, 0.432)		
Daytime functions	0.083 (-0.187, 0.341)	0.275* (0.010, 0.504)	
Parasomnias	0.454*** (0.214,0.642)	0.138 (-0.133, 0.389)	0.178 (-0.092, 0.424)

Note- *** = p < .01 level, * = p < .05 level.

Table 5.21 *Correlation between REDUCED CASS factor scores non-ADHD group (N=48). Spearman's rho and confidence intervals have been presented.*

Domain	Sleep problems and impacts	Executive and sensory regulation	Daytime functions
Executive and sensory regulation	0.588*** (0.358, 0.751)		
Daytime functions	0.505*** (0.249, 0.694)	0.346* (0.059, 0.579)	
Parasomnias	0.481*** (0.220,0.678)	0.457** (0.190, 0.661)	0.298* (0.007, 0.543)

Note- *** = p < .01 level, * = p < .05 level, ** = p < .01 level.

Reliability Analysis of the Reduced CASS Scale

Reliability analysis was re-conducted on the reduced CASS scale which consisted of 19 items. Cronbach's Alpha for the tool was computed to be @ = 0.897 indicating good reliability. Table 5.22 shows Cronbach's Alpha values for each of the reduced CASS factors for the combined sample, ADHD, and non-ADHD groups. Results demonstrate values ranging above 0.6 for all domains.

Table 5.22. *Cronbach's Alpha of REDUCED CASS scale factors for combined ADHD and Non-ADHD groups.*

Scale (n items)	COMBINED N= 106	ADHD N= 58	NON-ADHD N=48
Sleep problems and impacts (7)	0.916	0.877	0.914
Executive and sensory regulation (6)	0.761	0.627	0.800
Daytime functions (3)	0.779	0.806	0.740
Parasomnias (3)	0.745	0.649	0.837

Table 5.23 presents the test-retest reliability for reduced CASS scores between Time 1 and Time 2 for parents of children with or without ADHD and the combined sample results. Values represent strong correlations indicating good test-retest reliability. Figure 5.6 presents the correlation between the reduced CASS total scores for time 1 and time 2.

Table 5.23. *Test-retest reliability correlation coefficient between Time 1 and Time 2 REDUCED CASS scores for parents of children with or without ADHD. Spearman's rho values and confidence intervals have been presented. (ADHD Time 1 n=58, ADHD Time 2 n= 42, non-ADHD Time 1 n=48, non-ADHD Time 2 n= 27)*

CASS domains	COMBINED	ADHD	NON-ADHD
REDUCED CASS total	0.817*** (0.716, 0.885)	0 .739*** (0.639, 0.886)	0.791*** (0.580, 0.903)
SLEEP PROBLEMS AND IMPACTS	0.833*** (0.739, 0.895)	0.765*** (0.594, 0.869)	0.883*** (0.752, 0.947)
EXECUTIVE AND SENSORY REGULATION	0.723*** (0.582, 0.822)	0.640*** (0.410, 0.794)	0.769*** (0.542, 0.892)
DAYTIME FUNCTIONS	0.793*** (0.681,0.869)	0.844*** (0.722, 0.915)	0.691*** (0.411, 0.851)
FACTOR4	0.793*** (0.681, 0869)	0.847*** (0.727, 0.917)	0.644*** (0.339, 0.826)

Note- *** = p < .001 level.

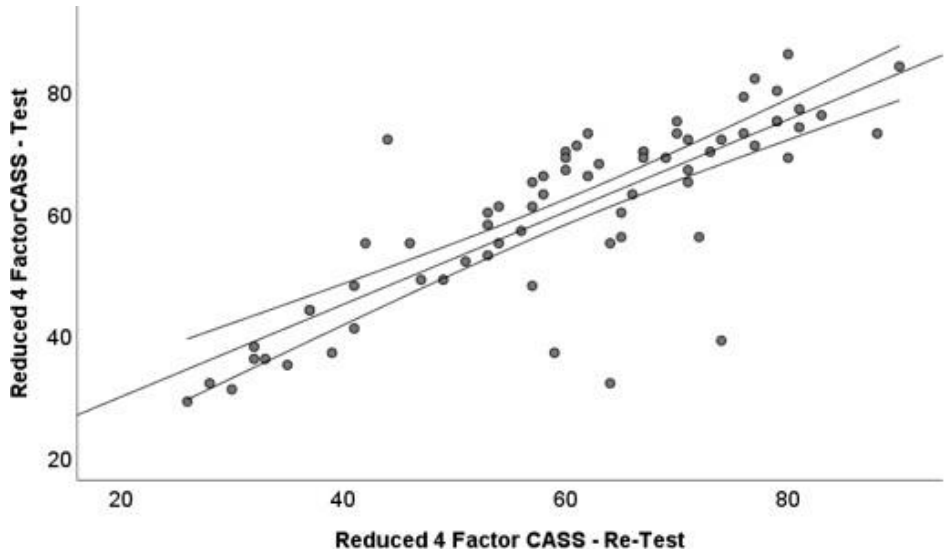


Figure 5.6 *Scatterplot showing the correlation between Time 1 and Time 2 Reduced CASS total scores.*

A two-way repeated measures ANOVA was performed to determine whether any change in reduced CASS total score is the result of the interaction between ADHD diagnosis category and time. There was a statistically significant effect of ADHD diagnosis on reduced CASS total scores (F (1,67) = 22.93, p = < 0.001), however no interaction effect of ADHD diagnosis and time (p = 0.95) or no main effect of time was present (p = 0.94). Figure 5.7 shows the above significant effect.

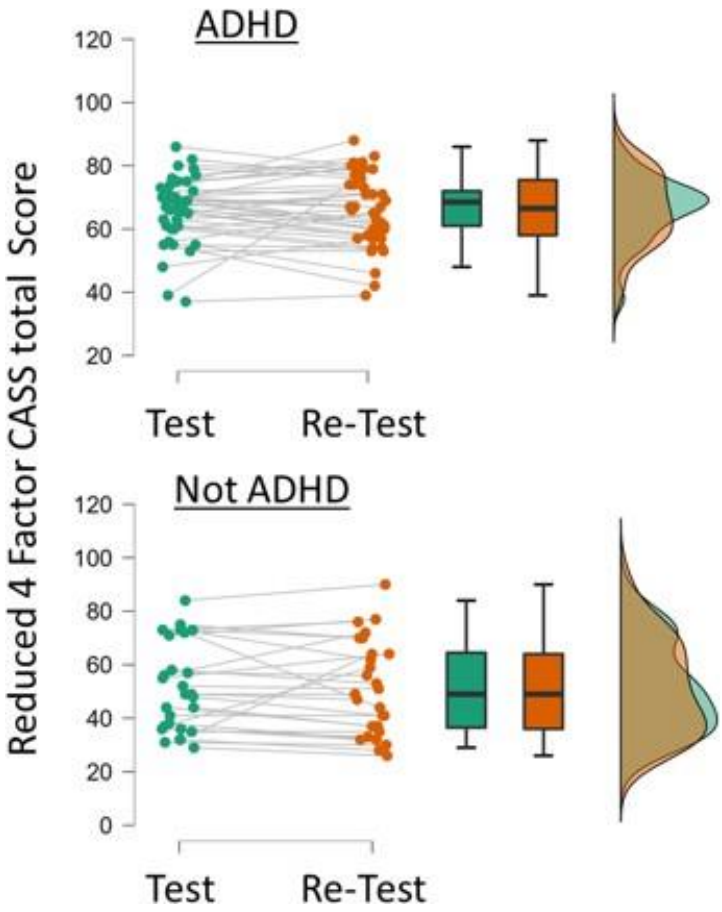


Figure 5.7 *Effect of ADHD diagnosis on reduced CASS total scores across Time 1 and Time 2*

Correlation analysis of CSHQ scores with CASS and reduced CASS

Tables 5.24, 5.25, 5.26 show the Spearman correlation coefficients between CASS domains and CSHQ domains for the combined, ADHD and non-ADHD groups respectively. Results show the following trends (associations significant @ 0.001, 0.01 and 0.05 level):

1. Bedtime domain was found to be strongly associated with CSHQ domains of Bedtime resistance (rho = 0.684), Sleep onset delay (rho = 0.605) and Sleep Anxiety (rho = 0.624). This relationship was similar for the non-ADHD, and the ADHD group, however overall the magnitude of association was lower for the ADHD group (Bedtime resistance, rho = 0.537, Sleep onset delay, rho = 0.327 and Sleep Anxiety rho = 0.433) than the non-ADHD group (Bedtime resistance, rho = 0.756), Sleep onset delay, rho = 0.660 and Sleep Anxiety rho = 0.771).
2. Sleep quality domain was found to be strongly associated with CSHQ domains of Bedtime resistance (rho = 0.601), Sleep onset delay (rho = 0.523), Sleep Anxiety (rho = 0.592), Night waking (rho = 0.619), Parasomnias (rho = 0.575) and Sleep duration (rho = 0.563). Similar associations were for the non-ADHD group, however for the ADHD group Sleep onset delay did not show any association with the CASS sleep quality domain..
3. Behaviour in sleep domain was most strongly associated with the CSHQ domain of Parasomnias (rho = 0.854) among the other domains. However for the ADHD group, Behaviour in sleep was only associated with Parasomnias and Sleep duration (rho = 0.818 and rho = 0.439 respectively).
4. Daytime functions domain was most strongly associated with Daytime sleepiness (rho = 0.625). Similar associations were found for the ADHD and the non-ADHD groups.

5. Impacts on family was found to be strongly associated with CSHQ domains of Bedtime resistance (rho = 0.690), Sleep onset delay (rho = 0.585) and Sleep Anxiety (rho = 0.643). Night waking (rho = 0.567), Parasomnias (rho = 0.529) and Sleep duration (rho = 0.620). Similar associations were found for the ADHD and the non-ADHD groups.

Tables 5.28, 5.29, 5.30 show the Spearman correlation coefficients between reduced CASS and CSHQ for the combined, ADHD and non-ADHD groups. Results show the following associations (P< 0.001, 0.01 and 0.05 level):

1. Sleep Problems and Impacts factor was found to be strongly associated with CSHQ Bedtime resistance (rho = 0.665), Sleep onset delay (rho = 0.587), Sleep Anxiety (rho = 0.627), Night waking (rho = 0.674), Parasomnias (rho = 0.567) and Sleep duration (rho = 0.648). These associations were similar for the non-ADHD, and the ADHD group, however for the ADHD group Sleep onset delay did not show any association with this factor
2. Executive and sensory regulation factor was found to be well associated with CSHQ domains of Bedtime resistance (rho = 0.577), Sleep onset delay (rho = 0.420), Sleep Anxiety (rho = 0.502), and Parasomnias (rho = 0.321). These associations were widespread across all CSHQ domains for the non-ADHD group, however for the ADHD group, none of the CSHQ domains were correlated with this factor of the reduced CASS
3. Daytime functions factor was most strongly associated with the CSHQ Daytime sleepiness (rho = 0.771). A similar association was found for the non-ADHD and ADHD groups.

4. Parasomnias factor from the reduced CASS was most strongly associated with CSHQ Parasomnias (rho = 0.764). Similar associations were found for the ADHD and non-ADHD groups.

Table 5.24 *Correlation between CASS scores and CSHQ scores for combined group (N=107). Spearman's rho and confidence intervals have been presented.*

CASS	CSHQ total	Bedtime Resistance	Sleep onset delay	Sleep Anxiety	Night wakings	Parasomnias	Sleep disordered breathing	Daytime Sleepiness	Sleep Duration
CASS TOTAL	0.870*** (0.813, 0.911)	0 .704*** (0.588, 0.791)	0.592*** (0.446, 0.706)	0.686*** (0.566, 0.778)	0.567*** (0.416, 0.687)	0.673*** (0.548, 0.768)	0.399*** (0.219, 0.552)	0 .412*** (0.234, 0.564)	0.596*** (0.452, 0.710)
BEDTIME	0.710*** (0.596, 0.796)	0.684*** (0.563, 0.766)	0.605*** (0.463, 0.717)	0.624*** (0.487, 0.731)	0.396*** (0.215, 0.550)	0.415*** (0.237, 0.566)	0.265** (0.072, 0.439)	0.320*** (0.131, 0.487)	0.497*** (0.332, 0.632)
SLEEP QUALITY	0.812*** (0.733, 0.870)	0.601*** (0.458, 0.714)	0.523*** (0.363, 0.653)	0.592*** (0.447, 0.707)	0.619*** (0.480, 0.727)	0.575*** (0.426, 0.694)	0.327*** (0.139, 0.492)	0.444*** (0.271, 0.590)	0.563*** (0.412, 0.684)
BEHAVIOUR IN SLEEP	0.658*** (0.530,0.757)	0.453*** (0.281, 0.597)	0.399*** (0.219, 0.553)	0.532*** (0.374,0.660)	0.448*** (0.275, 0.593)	0.854*** (0.790, 0.900)	0.400*** (0.220,0.553)	0.171 (-0.027, 0.356)	0.425*** (0.249, 0.574)
DAYTIME FUNCTIONS	0.637*** (0.504, 0741)	0.408*** (0.229, 0.560)	0.351*** (0.165, 0.513)	0.347*** (0.161, 0.510)	0.223* (0.027, 0.402)	0.385*** (0.204, 0.541)	0.296** (0.105, 0.466)	0.652*** (0.521, 0.752)	0.399*** (0.220, 0.553)
IMPACTS ON FAMILY	0.780*** (0.689, 0.847)	0.690*** (0.570, 0.781)	0.585*** (0.438, 0.701)	0.643*** (0.511, 0.746)	0.567*** (0.416, 0.687)	0.529*** (0.370, 0.657)	0.349*** (0.163, 0.511)	0.325*** (0.136, 0.490)	0.620*** (0.482, 0.728)

Note- Values significant @ ***p < .001 level, ** p < .01 level, * p < .05 level.

Table 5.25 *Correlation between CASS scores and CSHQ scores for ADHD group (N=59). Spearman's rho and confidence intervals have been presented.*

CASS	CSHQ total	Bedtime Resistance	Sleep onset delay	Sleep Anxiety	Night wakings	Parasomnias	Sleep disordered breathing	Daytime Sleepiness	Sleep Duration
CASS TOTAL	0.814*** (0.698, 0.888)	0 .577*** (0.366, 0.732)	0.316* (0.052, 0.538)	0.576*** (0.364, 0.731)	0.381** (0.126, 0.589)	0.568*** (0.355, 0.726)	0.322* (0.059, 0.543)	0 .261 (-0.007, 0.495)	0.604*** (0.401, 0.750)
BEDTIME	0.491*** (0.256, 0.670)	0.537*** (0.314, 0.703)	0.327* (0.064, 0.547)	0.433*** (0.187, 0.628)	0.084 (-0.189, 0.344)	0.173 (-0.099, 0.422)	0.109 (-0.164, 0.366)	0.116 (-0.157, 0.372)	0.373*** (0.117, 0.583)
SLEEP QUALITY	0.727*** (0.571, 0.833)	0.461*** (0.220, 0.649)	0.251 (-0.018, 0.486)	0.471*** (0.233, 0.656)	0.470*** (0.231, 0.655)	0.457*** (0.215, 0.646)	0.220 (-0.051, 0.461)	0.301* (0.036, 0.526)	0.540*** (0.318, 0.706)
BEHAVIOUR IN SLEEP	0.588*** (0.379,0.739)	0.297 (0.032, 0.523)	0.266 (-0.002, 0.498)	0.404 (0.153,0.606)	0.236 (-0.034, 0.474)	0.818*** (0.704, 0.891)	0.338 (0.077,0.555)	-0.020 (-0.287, 0.249)	0.439*** (0.194, 0.632)
DAYTIME FUNCTIONS	0.494*** (0.260, 0673)	0.157 (-0.116, 0.407)	- 0.012 (-0.279, 0.257)	0.104 (-0.168, 0.362)	0.038 (-0.232, 0.303)	0.113 (-0.159, 0.370)	0.124 (-0.149, 0.379)	0.646*** (0.457, 0.779)	0.239 (-0.031, 0.476)
IMPACTS ON FAMILY	0.692*** (0.521, 0.810)	0.564*** (0.349, 0.723)	0.360** (0.102, 0.573)	0.524*** (0.298, 0.694)	0.411** (0.160, 0.611)	0.403** (0.151, 0.605)	0.310* (0.046, 0.534)	0.191 (-0.081, 0.437)	0.579*** (0.396, 0.733)

Note- Values significant @ ***p < .001 level, ** p < .01 level, * p < .05 level.

Table 5.26 *Correlation between CASS scores and CSHQ scores for non-ADHD group (N=48). Spearman's rho and confidence intervals have been presented.*

CASS	**CSHQ total**	**Bedtime Resistance**	**Sleep onset delay**	**Sleep Anxiety**	**Night wakings**	**Parasomnias**	**Sleep disordered breathing**	**Daytime Sleepiness**	**Sleep Duration**
CASS TOTAL	0.901*** (0.827, 0.945)	0 .759*** (0.600, 0.860)	0.663*** (0.460, 0.800)	0.749*** (0.584, 0.854)	0.619*** (0.399, 0.771)	0.658*** (0.453, 0.797)	0.402** (0.124, 0.621)	0 .584*** (0.352, 0.749)	0.607*** (0.383, 0.764)
BEDTIME	0.825*** (0.702, 0.900)	0.756*** (0.596, 0.859)	0.660*** (0.456, 0.798)	0.771*** (0.618, 0.868)	0.486*** (0.204, 0.669)	0.474*** (0.211, 0.673)	0.346** (0.060, 0.579)	0.537*** (0.291, 0.717)	0.577*** (0.342, 0.744)
SLEEP QUALITY	0.834*** (0.716, 0.905)	0.658*** (0.453, 0.797)	0.574*** (0.338, 0.741)	0.631*** (0.415, 0.779)	0.664*** (0.461, 0.801)	0.533*** (0.286, 0.714)	0.356* (0.071, 0.587)	0.585*** (0.353, 0.749)	0.569*** (0.332, 0.738)
BEHAVIOUR IN SLEEP	0.637*** (0.423,0.783)	0.506*** (0.251, 0.696)	0.403** (0.126, 0.622)	0.558*** (0.318,0.731)	0.541*** (0.296, 0.719)	0.817*** (0.689, 0.895)	0.388** (0.109,0.611)	0.283 (-0.010, 0.531)	0.337* (0.050, 0.573)
DAYTIME FUNCTIONS	0.726*** (0.550, 0.840)	0.596*** (0.368, 0.756)	0.572*** (0.336, 0.740)	0.529*** (0.280, 0.711)	0.270 (-0.024, 0.521)	0.508*** (0.253, 0.697)	0.454** (0.187, 0.659)	0.662*** (0.459, 0.800)	0.495*** (0.237, 0.688)
IMPACTS ON FAMILY	0.778*** (0.629, 0.872)	0.726*** (0.551, 0.840)	0.604*** (0.378, 0.762)	0.703*** (0.517, 0.825)	0.575*** (0.340, 0.742)	0.473*** (0.210, 0.672)	0.308* (0.018, 0.551)	0.454** (0.187, 0.659)	0.576*** (0.342, 0.743)

Note- Values significant @ ***p < .001 level, ** p < .01 level, * p < .05 level.

Table 5.27 *Correlation between CASS scores and Brown EFA scores for combined group (N=107). Spearman's rho and confidence intervals have been presented.*

VARIABLES	Brown EFA total score	Activation	Focus	Effort	Emotion	Memory	Action
CASS TOTAL	0.755*** (0.656, 0.828)	0 .749*** (0.649, 0.824)	0.685*** (0.565, 0.777)	0.764*** (0.668, 0.835)	0.710*** (0.597, 0.795)	0.672*** (0.549, 0.767)	0.693*** (0.575, 0.783)
BEDTIME	0.732*** (0.626, 0.812)	0.710*** (0.597, 0.795)	0.687*** (0.567, 0.778)	0.742*** (0.639, 0.819)	0.688*** (0.568, 0.779)	0.672*** (0.548, 0.767)	0.712** (0.599, 0.797)
SLEEP QUALITY	0.659*** (0.531, 0.757)	0.660*** (0.533, 0.758)	0.577*** (0.429, 0.694)	0.682*** (0.561, 0.775)	0.629*** (0.493, 0.734)	0.559*** (0.408, 0.681)	0.579*** (0.432, 0.696)
BEHAVIOUR IN SLEEP	0.507*** (0.345,0.640)	0.510*** (0.349, 0.642)	0.474*** (0.306, 0.613)	0.501*** (0.338,0.635)	0.419*** (0.242, 0.568)	0.473*** (0.305, 0.612)	0.469*** (0.300,0.609)
DAYTIME FUNCTIONS	0.486*** (0.321, 0623)	0.535*** (0.379, 0.662)	0.428*** (0.253, 0.576)	0.542*** (0.387, 0.668)	0.483* (0.317, 0.621)	0.382*** (0.201, 0.538)	0.436** (0.263, 0.583)
IMPACTS ON FAMILY	0.616*** (0.477, 0.725)	0.615*** (0.476, 0.724)	0.553*** (0.400, 0.676)	0.612*** (0.472, 0.721)	0.582*** (0.436, 0.699)	0.555*** (0.402, 0.677)	0.591*** (0.446, 0.705)

Note- Values significant @ ***p < .001 level, ** p < .01 level, * p < .05 level.

Table 5.28 *Correlation between REDUCED CASS total scores and CSHQ scores for combined group (N=105). Spearman's rho and confidence intervals have been presented.*

Reduced CASS factors	**CSHQ total**	**Bedtime Resistance**	**Sleep onset delay**	**Sleep Anxiety**	**Night wakings**	**Parasomnias**	**Sleep disordered breathing**	**Daytime Sleepiness**	**Sleep Duration**
REDUCED CASS total	0.870*** (0.812, 0.911)	0 .720*** (0.609, 0.803)	0.589*** (0.443, 0.704)	0.672*** (0.547, 0.767)	0 .564*** (0.413, 0.685)	0.618*** (0.479, 0.727)	0.393*** (0.212, 0.547)	0 .456*** (0.285, 0.600)	0.578*** (0.430, 0.696)
SLEEP PROBLEMS AND IMPACTS	0.793*** (0.706, 0.856)	0.665*** (0.539, 0.762)	0.587*** (0.441, 0.703)	0.627*** (0.490, 0.733)	0.647*** (0.516, 0.749)	0.567*** (0.417, 0.687)	0.336*** (0.149, 0.500)	0.282 (0.090, 0.454)	0.648*** (0.517, 0.750)
EXECUTIVE AND SENSORY REGULATION	0.574*** (0.424, 0.692)	0.577*** (0.429, 0.695)	0.420*** (0.243, 0.570)	0.502*** (0.338, 0.636)	0.283 (0.090, 0.454)	0.321*** (0.132, 0.488)	0.305 (0.114, 0.473)	0.312 (0.122, 0.480)	0.266 (0.073, 0.440)
DAYTIME FUNCTIONS	0.517*** (0.356,0.648)	0.270** (0.077, 0.444)	0.363*** (0.179, 0.523)	0.177 (-0.020,0.362)	0.069 (-0.130, 0.263)	0.152 (-0.047, 0.339)	0.121 (-0.078,0.310)	0.771*** (0.677, 0.841)	0.325*** (0.137, 0.491)
PARASOMNIAS	0.604*** (0.462, 0716)	0.423*** (0.247, 0.573)	0.387*** (0.206, 0.543)	0.511*** (0.349, 0643)	0.380*** (0.198, 0.537)	0.764*** (0.668, 0.835)	0.279 (0.086, 0.451)	0.170 (-0.028, 0.356)	0.360*** (0.175, 0.520)

Note- Values significant @ ***p < .01 level, ** p < .01 level.

Table 5.29. *Correlation between REDUCED CASS total scores and CSHQ scores for ADHD group (N=58). Spearman's rho and confidence intervals have been presented.*

Reduced CASS factors	**CSHQ total**	**Bedtime Resistance**	**Sleep onset delay**	**Sleep Anxiety**	**Night wakings**	**Parasomnias**	**Sleep disordered breathing**	**Daytime Sleepiness**	**Sleep Duration**
REDUCED CASS total	0.806*** (0.686, 0.883)	0 .603*** (0.400, 0.750)	0.309 (0.045, 0.533)	0.553*** (0.335, 0.715)	0 .368** (0.111, 0.579)	0.452*** (0.210, 0.642)	0.300* (0.035, 0.556)	0 .338* (0.078, 0.600)	0.573*** (0.360, 0.729)
SLEEP PROBLEMS AND IMPACTS	0.672*** (0.493, 0.796)	0.526*** (0.300, 0696)	0.301 (0.037, 0.527)	0.428*** (0.246, 0.664)	0.524*** (0.298, 0.694)	0.445*** (0.201, 0.637)	0.298* (0.023, 0.517)	0.071 (-0.201, 0.332)	0.637*** (0.445, 0.773)
EXECUTIVE AND SENSORY REGULATION	0.339 (0.078, 0.556)	0.416 (0.166, 0.615)	0.159 (-0.114, 0.409)	0.287 (0.021, 0.515)	0.049 (-0.222, 0.313)	0.038 (-0.232, 0.303)	0.152 (-0.121, 0.403)	0.126 (-0.147, 0.381)	0.081 (-0.191, 0.342)
DAYTIME FUNCTIONS	0.450 (0.207,0.641)	0.066 (0.626, 0.328)	0.242 (-0.028, 0.479)	0.027 (-0.243,0.292)	-0.160 (-0.411, 0.113)	0.031 (-0.238, 0.297)	-0.025 (-0.291,0.244)	0.769*** (0.630, 0.859)	0.238 (-0.032, 0.475)
PARASOMNIAS	0.572*** (0.360, 0729)	0.318 (0.016, 0.540)	0.314 (0.050, 0.537)	0.394 (0.141, 0.599)	0.220 (-0.051, 0.461)	0.724*** (0.566, 0.831)	0.219 (0.460, -0.052)	-0.028 (-0.294, 0.242)	0.411*** (0.161, 0.612)

Note- Values significant @ ***p < .01 level, ** p < .01 level.

Table 5.30 *Correlation between REDUCED CASS total scores and CSHQ scores for Non-ADHD group (N=48). Spearman's rho and confidence intervals have been presented.*

Reduced CASS factors	**CSHQ total**	**Bedtime Resistance**	**Sleep onset delay**	**Sleep Anxiety**	**Night wakings**	**Parasomnias**	**Sleep disordered breathing**	**Daytime Sleepiness**	**Sleep Duration**
REDUCED CASS total	0.893*** (0.813, 0.940)	0 .755*** (0.594, 0.858)	0.652*** (0.445, 0.793)	0.736*** (0.565, 0.846)	0 .588*** (0.358, 0.751)	0.617*** (0.397, 0.770)	0.412*** (0.137, 0.629)	0 .622*** (0.403, 0.774)	0.579*** (0.345, 0.745)
SLEEP PROBLEMS AND IMPACTS	0.798*** (0.660, 0.884)	0.677*** (0.480, 0.809)	0.624*** (0.407, 0.775)	0.673*** (0.474, 0.806)	0.664*** (0.462, 0.801)	0.520*** (0.269, 0.705)	0.301* (0.010, 0.545)	0.449** (0.181, 0.655)	0.611*** (0.388, 0.766)
EXECUTIVE AND SENSORY REGULATION	0.682*** (0.488, 0.813)	0.652*** (0.444, 0.793)	0.514*** (0.261, 0.701)	0.642*** (0.431, 0.787)	0.319* (0.030, 0.559)	0.411** (0.136, 0.628)	0.372** (0.090, 0.599)	0.480*** (0.219, 0.677)	0.382** (0.102, 0.607)
DAYTIME FUNCTIONS	0.644*** (0.433,0.788)	0.481*** (0.219, 0.678)	0.504*** (0.248, 0.694)	0.339* (0.052,0.574)	0.274 (-0.019, 0.524)	0.231 (-0.066, 0.490)	0.327 (0.039,0.565)	0.762*** (0.604, 0.862)	0.440** (0.169, 0.648)
PARASOMNIAS	0.619*** (0.399, 0772)	0.492*** (0.234, 0.686)	0.369* (0.086, 0.596)	0.579*** (0.345, 0.745)	0.494*** (0.237, 0.687)	0.780*** (0.633, 0.873)	0.285 (-0.008, 0.533)	0.318* (0.029, 0.558)	0.309* (0.018, 0.551)

Note- Values significant @ ***p < .01 level, ** p < .01 level.

Table 5.31 *Correlation between REDUCED CASS total scores and Brown EFA scales for combined group (N=106). Spearman's rho and confidence intervals have been presented.*

Reduced CASS factors	Brown EFA total score	Activation	Focus	Effort	Emotion	Memory	Action
REDUCED CASS total	0.706*** (0.592, 0.792)	0 .715*** (0.603, 0.799)	0.626*** (0.490, 0.732)	0.718*** (0.607, 0.801)	0.652*** (0.523, 0.752)	0.617*** (0.479, 0.726)	0.673*** (0.550, 0.768)
SLEEP PROBLEMS AND IMPACTS	0.634*** (0.500, 0.739)	0.640*** (0.507, 0.743)	0.572*** (0.423, 0.691)	0.641*** (0.509, 0.744)	0.594*** (0.450, 0.707)	0.565*** (0.414, 0.685)	0.606*** (0.465, 0.717)
EXECUTIVE AND SENSORY REGULATION	0.610*** (0.470, 0.720)	0.552*** (0.399, 0.675)	0.599*** (0.456, 0.711)	0.602*** (0.460, 0.714)	0.571*** (0.423, 0.690)	0.585*** (0.439, 0.701)	0.599*** (0.457, 0.712)
DAYTIME FUNCTIONS	0.312 (0.123,0.479)	0.399*** (0.220, 0.552)	0.219 (0.024, 0.398)	0.397* (0.218,0.550)	0.268 (-0.075, 0.441)	0.188 (-0.008, 0.371)	0.276 (0.084,0.448)
PARASOMNIAS	0.463*** (0.262, 0582)	0.440*** (0.267, 0.586)	0.396*** (0.216, 0.549)	0.433*** (0.258, 0.580)	0.393*** (0.213, 0.547)	0.371*** (0.189, 0.529)	0.410*** (0.232, 0.561)

Note- Values significant @ ***p < .01 level, ** p < .01 level.

5.4 Discussion

Sleep disturbances such as bedtime refusal, difficulty initiating, maintaining, and transitioning from sleep to waking state, breathing disorders and periodic limb movements, sleep fragmentation, and increased levels of daytime sleepiness are commonly reported in children diagnosed with ADHD (Bondopadhyay et al 2021; Cortese et al 2009; Díaz-Román et al., 2016, and Yoon et al 2012). Sleep problems and ADHD symptoms mutually exacerbate each other and present themselves bidirectionally within the child's clinical picture, thereby justifying the need to pay clinical attention to both these concerns (Hysing, 2013). Pharmacological interventions such as the use of melatonin (Kimland et al 2021, Abdelgadir et al 2018) or non- pharmacological interventions such as sleep hygiene (Nickles et al 2020) and cognitive therapy (Bériault et al 2018) based interventions or the use of weighted blankets (Beresford et al 2018) have shown improvement in sleep and overall wellbeing of the child (Malkani et al 2022).

The need for an ADHD specific sleep questionnaire

The importance of assessing the presence of sleep disorders among children and adolescents with developmental disorders and affective disorders has been previously highlighted (Arns et al 2021). Cortese et al. (2013) iterated that to aid effective management for sleep problems for children with ADHD, an accurate differential diagnosis by the clinician is imperative, for which they recommended a sleep assessment protocol. Baseline assessment and systematic screening for sleep problems were recommended for which a 5 item instrument BEARS (B = Bedtime issues, E = Excessive daytime sleepiness, A = night Awakenings, R = Regularity and duration of sleep, S = Snoring) (Owens and Dalzell, 2005) was mentioned and more detailed report using the Child Sleep Habits Questionnaire (CSHQ) (Owens et al 2000) was recommended, followed by the use of a sleep diary and if warranted, specific objective

investigation of sleep properties through the use of Polysomnography or actigraphy (Cortese et al 2013). The above discussed article indicates that sleep assessment questionnaires designed for general paediatric populations such as Child Sleep Habits Questionnaire (CSHQ) (Owens et al 2000), Pediatric Sleep Questionnaire (PSQ) (Chervin et al 1997), Child Sleep Wake Scale (CSWS) (LeBourgeois and Harsh, 2001) or Sleep Disturbance Scale for Children (SDSC) (Bruni et al 1996) are generally used for research and clinical practice with this population, although these scales do not capture ADHD specific sleep problems. Although CSHQ is one of the most commonly utilized tool for pediatric sleep assessment, especially in research, Markovich et al (2014) found no correlation between CSHQ subscales and Polysomnography scores and had low construct and diagnostic validity. This does open the debate for use of other tools the Holland Sleep Disorder Questionnaire (HSDQ) (Kerkhof et al 2013) that was validated against polysomnography, in order to reach diagnostic accuracy.

The relevance of a condition specific sleep assessment tool was recognised previously when the Family Inventory of Sleep Habits (FISH was developed to assess sleep in Autism Spectrum Disorder (ASD) (Malow et al 2009)) and the Modified Simonds and Parraga Sleep Questionnaire (MSPSQ) for use with intellectual disability patients was developed (Simonds and Parraga, 1982, Wiggs and Stores, 1996; Wiggs and Stores, 1998; Wiggs and Stores, 2004). The MSPSQ was also found useful to assess sleep for children with ASD (Johnson et al 2012). In these questionnaires, common sleep problems mentioned in the above discussed multidimensional sleep questionnaires were modified to match the core autism symptoms, for example sensory processing needs during sleep and anxiety associated with emotional arousal during night wakings or nightmares (Johnson et al 2012). Similarly, considering childhood ADHD symptoms have a substantial impact on the child's daily activities (Frye et al 2018; Becker et al 2018), these would also have an effect on their sleep and behaviours leading up to sleep (Frick et al 2022). This suggests that from a clinical perspective, a tool specifically

designed to assess sleep disturbances in childhood ADHD would therefore be of utility.

Development of CASS

We developed a parent-rated sleep assessment questionnaire to evaluate sleep problems in children with ADHD, the Childhood ADHD Sleep Scale (CASS). The term 'sleep problems' in childhood ADHD can be a series of non-specific sleep related concerns, caused by a comorbid sleep disorder or poor sleep practices or psychiatric comorbidities or medical disorder or medications or the symptoms of ADHD (or a combination of two or more of these reasons) (Cortese et al 2013). CASS therefore included multidimensional sleep domains, with items attempting to capture the above-mentioned reasons for the presence of sleep problems. For example, in the domain of Bedtime, although bedtime resistance was explored (often reported in this population; Kirov, 2011), ADHD-specific emotional, behavioural, cognitive dysregulation (Chutko et al 2022) or the role of comorbid psychopathology (Xia et al 2015) or poor sleep practices (Martin et al 2020) were incorporated within the items. Further, for the sleep quality domain, although sleep maintenance and quality was explored, items also included questions about child asking parent reassurance (as reported in this population, Becker 2020) or having a poorer sleep on school days (Becker et al 2019) or having a ADHD specific comorbidity related sleep issue (for example, wake timing rigidity associated with comorbid ASD symptoms).

The daytime functions domain included items pertaining to daytime sleepiness (following a poor night's sleep), but also incorporated items related worse emotional/behavioural/attentional outcomes for the next day (Cassoff et al 2012). Parasomnias reported in ADHD (Eyuboglu and Eyuboglu, 2017), formed the Behaviours in sleep domain. Impacts on family, was a completely ADHD specific domain exploring sleep related or behavioural consequences of child's sleep issues faced by the parent (et al 2020; Sung et al 2008). Hence, the original prototype of CASS including the 5 domains of Bedtime, Sleep

Quality, Behaviours during sleep, Daytime functions and Impacts on family, incorporated ADHD specific sleep problems, which are not captured by widely used pediatric sleep questionnaires. Using such an ADHD specific sleep tool can reduce the need for administering multiple stages of assessment (i.e. BEARS, followed by CSHQ, followed by Sleep Diary) from the above mentioned sleep assessment protocol (Cortese et al 2013).

Questions pertaining to the effect of medication.

Stimulant medication (such as Methylphenidate hydrochloride (MPH)) is the most widely used pharmacological treatment for children with ADHD (Safer, 2016). Corkum et al (2020) explained that MPH facilitates the release of Dopamine (DA) and Norepinephrine (NE) from the presynaptic membrane and blocks the reuptake of DA and NE by their transporters, resulting in increased availability and action of these neurotransmitters in the prefrontal cortex and Striatum, thereby facilitating improved neurocognitive functions (Enger and Pruessner, 2008). Inconsistent literature about the impact of stimulant medication, with some studies reporting worse sleep (longer sleep latency, shorter sleep duration or worse sleep efficiency) for ADHD children on these medications (Kidwell et al 2015), while other studies report the beneficial effects of medication in improving the quality of sleep in these children (Tomas Vila et al 2010; Velez Galarraga et al 2016).

Information pertaining to the parent's perception on how medication might have impacted their child's sleep can provide a comprehensive account of information to the clinician. Such information can be utilised to modify the formulation, dosage, and time of day administration to optimise performance and minimise sleep impacts. Current research examining the effect of stimulants have mostly studied immediate release formulations (Corkum et al 2008; Galland et al 2010; Sangal et al 2006), however delayed release which have longer effect on performance might also incur a prolonged effect on sleep (Faraone and Glatt, 2010). As such, formulations and timing of the drug administration can be effectively

modified through CASS. Widely used multidimensional sleep tools such as CSHQ would not provide such detailed treatment specific information to the clinician. CASS includes four descriptive adjuncts which explore the perceived effect of ADHD medication on the child's sleep, including effect of Melatonin (if used in addition to the stimulant or by itself). Melatonin plays a key role in regulating the body's circadian rhythm (Gordon, 2000) and has demonstrated both hypnotic and chronobiotic properties (Wirz- Justice and Armstrong, 1996), improving sleep wake rhythm problems and reducing sleep latency (Appleton et al 2013; Anand et al 2017).

Properties of CASS

The current pilot study has explored the psychometric properties of Childhood ADHD Sleep Scale (CASS), a parent rated questionnaire that investigates sleep in their children diagnosed with ADHD. The overall internal consistency of the CASS was found to be excellent, and all five domains demonstrated acceptable reliability measure. Although the combined and non-ADHD sample demonstrated acceptable and good reliability the ADHD participants (for the domains of Bedtime, Sleep quality and Daytime functions) showed lower values. As test -retest reliability is influenced by the dynamic nature of the construct being measured (Haynes et al., 2018), this change might be more susceptible within the clinical population due to varying social-emotional–sensory responses and their impacts between the questionnaire administration time intervals. For the combined sample, CASS demonstrated good internal validity and indicated that results obtained over time are stable.

While listing and wording items of the scale, the authors gave careful consideration to current research and findings from the author's previous qualitative study which explored sleep related difficulties as observed by parents of children diagnosed with ADHD (2022, under peer review). CASS items were created with joint consideration to the above constructs, and the

‘gold standard’ of childhood sleep questionnaire, that is Child Sleep Habits Questionnaire (CSHQ, Owens 2000), which is widely used as a subjective parent rated tool in child sleep research (Bondopadhyay et al 2021).

The Reduced CASS

Exploratory factor analysis of the original CASS led to formation of the reduced CASS tool comprising 4 factors. These factors included Sleep Problems and Impacts; Executive and Sensory Regulation; Daytime Functions; and Parasomnias. The overall internal consistency of the reduced CASS was found to be excellent. Test-retest reliability ranged between acceptable and good values with lower range for the ADHD group. The next section discusses ow the 5 original domains of CASS restructured themselves to form 4 new factors to assess sleep in the investigated group.

The Sleep problems and impacts domain were made up of items from the original CASS’s Sleep quality and Impacts on family and household domains. Apart from difficulty winding down to sleep and going to sleep, children with ADHD have been observed to have difficulty maintaining undisturbed sleep, returning to sleep after wakefulness and returning to functional wakefulness in the morning (Ball et al 1997; Corkum et al 2001; Kaplan et al 1987; Ring et al 1998; and Day and Abmayr 1998). Sleep dysfunctions in children with ADHD have been reported to detrimentally impact parental sleep, psychological problems, and the household (Buxton et al 2015). Sleep problems may be related to worsened parental wellbeing, which might then influence implementation of their parenting strategies to induce sleep in their child (Martin et al 2019). This domain of the scale broadly captures the items describing maintenance of sleep, returningh back to sleep and their impacts on parents and the family.

Executive and sensory regulation domain comprised of items from the original CASS’s Bedtime and Daytime function (1 item, effect of night when it was difficult to fall asleep)

domains. It is crucial to distinguish bedtime related sleep problems (including problems falling asleep or winding down) from maintenance of sleep (discussed in the last domain). Bedtime domain from the original CASS contained items related to executive functions which is the core area of deficit in ADHD (Barkley et al 1997). Certain ADHD subgroup populations with higher severity of executive function deficits and comorbid psychopathology may be more susceptible to sleep problems (Becker 2020) which in turn may adversely affect the core inattention/hyperactivity symptoms of ADHD (Goel et al 2009; Nilsson et al 2005). A recent study (Floros et al 2020) demonstrated that sleep loss influences cognitive conflict variability in individuals with ADHD, which thereby increases the difficulties in conflicting tasks requiring focus/action and response inhibition (Mansouri et al 2009). Winding down to sleep involves a number of night-time chores coupled with calming one's mind to fall asleep, which might be areas affected by deteriorated executive function skills. These areas are captured in this domain of the scale. This domain also consists of items describing sensory preferences of the child in the bedroom environment (light, temperature, or textures of bed items). Sensory processing problems, characterised by impaired detection, modulation and interpretation of sensory input have been previously found in the ADHD clinical picture (Ghanizadeh et al 2011). As responsivity to sensory stimulus can vary between hypersensitivity or hyposensitivity, sensory seeking tendency or problems with sensory discrimination (Miller et al 2007; Ben- Sasson et al 2008), this is translated to need based environments for the child specially to induce comfort during sleep.

The Daytime function domain was made up of original CASS's Sleep Quality (precisely how it effects morning functioning) and Daytime Function domains. Previous research has consistently demonstrated increased daytime sleepiness within the childhood ADHD clinical picture (Cortese et al 2006; Golan et al 2004; and LeBourgeois et al 2004). Daytime sleepiness may be an independent factor distinct from the child's sleep problems

(discussed in the first and second domain) (Lucas et al 2017). Langberg and colleagues (2013) showed that adolescent rated daytime sleepiness was associated with academic performance, but their sleep duration was not, which indicates that daytime sleepiness might be related to the daytime functioning in this population).

The Parasomnias domain comprised items from the original CASS's Behaviours in sleep domain. Parasomnias have previously been found in this population (Rodopman-Arman et al 2011), and within the scale, items retained included talking in sleep, nightmares and night terrors.

Descriptive comparison: Original CASS and CSHQ Vs reduced CASS and CSHQ

Although, an overlap of symptoms is apparent from the above description, its crucial to note that CASS is specifically designed to assess sleep problems corresponding to the ADHD clinical picture. Therefore, although the clinical signs of the sleep problem might resemble that of the CSHQ, the underlying construct that the scale measures are distinct. TheCSHQ is a widely used child sleep screening questionnaire designed for surveying sleep habits and disturbances (Owens et al 2000). Studies exploring sleep in childhood ADHD have extensively utilised CSHQ as a multidimensional parental reporting tool for sleep of children in this population (Bondopadhyay et al 2021). The nature of association between the original CASS and CSHQ and the reduced CASS and CSHQ further underlined how a distinct tool for assessing sleep problems in childhood ADHD is useful. While the original CASS's domains demonstrated multiple cross associations with the CSHQ domains, the reduced CASS structured withing the four factors revealed clearer pathways of association and most importantly the CSHQ did not show any association with the Executive and sensory regulation domain. This shows that executive dysfunctions and sensory processing variabilities which are characteristic ADHD symptoms influencing the individual's functioning (Schreiber et al 2014)

is not addressed within the CSHQ. Executive function deficits can cause lack of planning, and structuring activities, difficulty activating oneself and completing tasks and acting on established plans in addition to difficulty in flexible thinking and incorporating feedback (Anderson et al 2001); such processess may be crucial for healthy bedtime activities and night time schedules.

Strengths and Limitations

This is the first ADHD specific subjective assessment tool to assess sleep in pre-adolescent children. Not only is sleep foundational to an individual's physical, mental and social development (Mindell et al 2011), connections of sleep related problems with deficits in cognitive functions, attentional abilities, externalizing behaviours, progressive psychopathology and lack of emotional regulation (Matricciani et al 2012) have been demonstrated consistently. These behaviours mimic core symptoms of ADHD, thereby making sleep assessment imperative for a comprehensive management-based ADHD diagnostic protocol (Cortese et al 2013). Sleep hygiene (Peppers et al 2016; Hiscock et al 2015; Sciberras et al 2011) and behavioural intervention (Sciberras et al 2020; Keshavarzi et al 2014) for children diagnosed with ADHD have led to better functional outcomes in sleep quality, sleep duration, ADHD symptoms and quality of life. These findings substantiate the benefits of including sleep assessment as the first step in sleep-based intervention for ADHD management.

The domains of the CASS were designed based on previous qualitative research, thereby item selection and domain formation was based on empirical evidence. The generated themes of bedtime problems, steps taken by parents, impacts on the household and overall parent perspectives were considered while creating the items.CASS was validated against both CSHQ and a subjective (parent reported) measure of child's executive functions, thereby comprehensively involving ADHD specific measures in the analysis process. Recent studies

using large sample sizes, longitudinal and experimental research designs have created a robust and sophisticated developmental psychopathology framework-based understanding of the interplay of ADHD, sleep and general functioning (Meltzer, 2017). This literature has demonstrated that across the developmental years certain subgroups of individuals with ADHD may be at higher risk for developing sleep problems; for example those with severe executive function deficits or co-occurring internalizing psychopathology (Becker, 2020). Lewis et al (2022), demonstrated that greater polygenic liability for ADHD did not increase the risk of sleep disturbances in children with ADHD, thereby suggesting that there may be other factors (such as symptoms of ADHD, including executive function deficits), may make it difficulty for children to adopt healthy sleep practices. Acknowledging this novel viewpoint, we have incorporated a measure of executive functions to explore its association trends with those of the CASS domains.

Parents were specifically asked and requested to re-confirm whether their child was diagnosed with ADHD by a psychiatrist/psychologist/mental health professional, which led to the delopement of a clinical and control group. This reduced the risk of mixing responses from the clinical population with the control group. Test re-test reliability could be computed as the questionnaire was administered twice with an interval of 2 weeks, which therefore could demonstrate the stability of the measure when administered over two time periods

Our study has certain limitations. No diagnostic measure of ADHD was given for parent report, which could help determine the symptom presentation (inattentive, hyperactive/impulsive or combined). Of the studies conducted to examine sleep deficits in children with ADHD, most have included samples of participants diagnosed with ADHD combined presentation (Kirov et al 2007 and Yurumez and Bilic 2013). However, a growing body of research has established that ADHD- inattentive presentation (ADHD- I) is associated with more daytime sleepiness as compared to combined type (Mayes et al 2009 and Lecendreux

et al 2000). In addition, Mayes et al 2009 found that children with ADHD-I who had a comorbid internalizing disorder (such as anxiety) had more sleep problems compared to children with ADHD-I alone. These findings were reconfirmed by Becker et al (2016) who found that comorbid anxiety in addition to sluggish cognitive tempo or tired symptoms were most consistently related with poorer sleep functioning, thereby underlying the importance of recruiting participants as per their ADHD symptom presentations.

The presence of internalizing and externalizing behavioural problems and co-occurrence of psychological conditions in childhood ADHD has been previously associated with increased sleep problems in this population (Becker et al 2018). As such, ascertaining information about the presence of comorbid conditions could help reveal more granular information on how the ADHD specific sleep problem items in CASS interact with common ADHD comorbidities.

Biased responses from parent reported subjective questionnaires about sleep (Holzhausen et al 2021) underline the importance of objective measures of sleep functions (polysomnography (PSG) or actigraphy;Rundo and Downey, 2019). Our study did not use objective techniques like PSG or actigraphy, but cross validated CASS with only the CSHQ, which could possibly be subject to rater biases.

Our study conducted only the initial steps of exploratory factor analysis, and no confirmatory factor analysis was conducted which therefore restricted the investigation of causal associations among the latent and observable variables (Mueller and Hancock 2001). Although through EFA we reduced the number of scale items and underlined the optimal model in which the four factors could be structured, each item was free to load on each factor, thereby producing discrepancy between the derived and the theoretical model. A confirmatory factor

analysis would allow items to load only on the factors they were created to assess, thereby giving access to the fit of the data to the theory derived model (Mueller and Hancock, 2001).

Less than 100 parents participated for each group (ADHD and control), with a total of 106 participants. Conflicting opinions about how many people should participate in a validation study, have over the years included proposals such as 'rules of thumb' (10 participants for every question in the instrument, Everitt, 1975); a flat rule of 100 participants (Kline, 2014); or 50 as poor to 300 as acceptable and 1000 as excellent (Comrey and Ley, 1992). However, White (2022) in their systematic review examining sample sizes in quantitative instrument validation, proposed that in case of diagnosed patient populations, 250-350 participants would be appropriate. Although this was a pilot validation of the CASS, future efforts for validation of this instrument should include a larger sample size which would support generalizations of the psychometric properties. Moreover, the validation for similar subjective account of sleep instruments, such as CSHQ (Owen et al 2000), the sample size was 469 for typically functioning children and parents of 154 children diagnosed with sleep disorders.

As sleep related behaviour and architecture evolve from infancy through childhood and the social context in which a child's sleep occurs in different ages might vary, a developmentally appropriate assessment of sleep is necessary especially in case of caregiver reports (Lewandowski et al 2020). CASS was primarily designed for use with preadolescent children between the age of 6-12 years. Including an older age sample, would allow us to capture the age related changes in sleep specific to ADHD (Wajszilber et al 2018). Moreover, even within the age range of 6-12 years, practical differences in sleep issues could be common, for example a 6 year old is more likely to be afraid of the dark, while a 12 year old would be anxious about a emotionally challenging situation, when trying to sleep without reassurance of a caregiver. Therefore, although the manifest problem of both the ages is delayed sleep onset,

the reason behind them might not be similar. Acknowledging such differences, age group wise analysis would lead to more robust results. This is strongly recommended in future studies.

More parents of boys participated in the study than girls, thereby leading to a less diverse gender make-up of the sample. As gender based variation in sleep functions (Acebo et al., 1996; Sadeh et al., 2000), circadian rhythm markers (Boivin et al., 2016; Cain et al., 2010; Duffy et al., 2011; Santhi et al., 2016) as well as ADHD clinical pictures (Rucklidge, 2010; Biederman et al 2002), are well established, a validation study for a ADHD specific instrument should include comparable number of male and female participants.

Future Directions

A future trial of the reduced CASS scale with a larger sample size and more specific items for each domain could be undertaken to prepare a functional version of the CASS. It is crucial that any future study with CASS should follow a guidance structure, for example Boateng et al., (2018) proposed 9 steps of scale development and validation. In this guiding structure, the first phase of item development includes identification of the domains and the content validity of the items; the second phase of scale development includes pre-testing of questions, administration of the survey, item reduction, and extraction of factors; and the third phase includes conducting tests of dimensionality, of reliability and validity (Boateng et al., 2018). Although for CASS, we attempted to follow selected steps from the three phases (such as identification of domains, survey administration, item reduction, factor extraction, tests of reliability and validity), a structured follow up of these stages chronologically would yield a comprehensive analysis of the tool. CASScan be of special clinical utility and has the potential to be a significant addition within the repertoire of tools for ADHD related functional assessment.

Chapter 6: Sleep-related attentional bias does not associate with symptoms of ADHD in a sample of younger adults.

Abstract

Sleep-related attentional bias, wherein exaggerated attention is directed to a sleep-related stimuli, has been proposed to be part of the cognitive processes that underpin the development and perpetuation of insomnia. Attention deficit hyperactivity disorder (ADHD) is commonly associated with clinically significant sleep disturbances, although the nature of the relationship between ADHD and sleep is not well understood. We hypothesised that ADHD symptoms would associate with greater attentional bias to sleep-related stimuli. We used an emotional Stroop task with sleep-related words to assess the presence of sleep attentional bias in a sample of 155 younger adults. ADHD symptoms and consistency with the presence of ADHD was assessed with the Adult ADHD Rating Scale- Self Report Screener and insomnia symptoms and probability for the presence of insomnia disorder was assessed with the Sleep Condition Indicator questionnaire. ADHD symptoms and consistency, and insomnia symptoms and probability for the presence of insomnia disorder were not found to associate with sleep attentional bias scores. Sleep attentional bias also did not associate with chronotype or social jetlag, but it was found that habitual use of an alarm clock on work days did associate with greater sleep attentional bias. As such, we did not find evidence to support the hypothesis that ADHD symptoms are associated with sleep attentional bias in a sample of healthy younger adults.

6.1 Introduction

Sleep-related attentional bias, an attentional preference to sleep-related stimulus, has been observed in individuals diagnosed with insomnia disorder (Harris et al, 2015 ;Lundh et al 1997; Taylor et al 2003; Jones, et al 2005; MacMahon, et al 2006; Barclay & Ellis 2013) and has also been observed to increase from the continuum of good quality to poor quality sleepers in non-clinical populations (Spiegelhalder et al. 2009). It has been postulated that attentional biases occur when individuals are more likely to selectively allot information processing resources to sensory input related to their concerns (for example, see Mogg & Bradley, 2005 for attentional biases in anxiety disorders & Cox et al 2004 for attentional bias in substance use disorders). Another proposed mechanism is the attention-intention-effort model, wherein sleep-related stimuli are more likely to induce threat or craving associated psychological reactions in patients with insomnia, as sleep-related stimuli might lead to recall of functional deterioration due to the disorder (threatening) or the need for sleep (craving) **(**Espie et al 2006). As such, sleep attentional biases have been proposed as an important feature of the cognitive model of insomnia: worry about sleep triggers autonomic arousal and emotional distress, which in turn triggers selective attention towards and monitoring of internal and external sleep-related threat cues (Harvey, 2002).

Sleep disturbances are reported to be common in attention deficit hyperactivity disorder (ADHD), with 70% of adults with ADHD reporting sleep-related concerns (Yoon et al 2012 and a prevalence of insomnia disorder of 44% has been reported in adults ADHD (Fadeuilhe et al. (2021). It has also been reported that clinical intervention for insomnia (psychoeducation/sleep hygiene, pharmacotherapy) in adult ADHD patients yielded improvement in ADHD symptoms, psychiatric comorbidities and overall quality of life after a 6 months follow up (Fadeuilhe et al, 2022). ADHD in adults is also associated with alterations in circadian rhythms in sleep-wake behaviours and molecular processes, including a marked

tendency towards later chronotype and habitual sleep timing (Coogan et al, 2019; Coogan and McGowan, 2017). It is not currently clear if changes in chronotype and circadian function are associated with attentional sleep biases: MacMahon et al (2006) have reported that patients with delayed sleep phase syndrome do not show greater sleep attentional biases, although there are no further reports in the literature on circadian rhythms and sleep attentional biases.

ADHD, as a disorder characterized by marked changes in attentional processes, may be associated with various attention biases. For example, there is evidence that ADHD is associated with an attentional bias against sad faces (Shapero et al, 2021), for alcohol (Roberts et al, 2012) and for both positive and negative emotional words (Shushakova et al, 2018). Because sleep disturbances, especially insomnia has been reported in adult ADHD populations (Fadeuilhe et al. 2021) and one important cognitive model for insomnia involves sleep attentional biases, where worrying about sleep, and the resultant autonomic arousal can make the individual pay selective attention to sleep related cues, we wanted to question whether a person with more ADHD related features will selectively allot attention to sleep related stimulus. There is no current examination of the presence of sleep attentional biases in either people with ADHD, or in relation to ADHD symptoms. As such, the current study tested the hypothesis that ADHD symptom severity in a non-clinical sample would associate with the presence of attentional sleep bias, and that the presence of insomnia symptoms would also associate with attentional sleep bias, and that the greatest attentional sleep bias would be present in participants with a combination of ADHD and insomnia symptoms. As secondary outcomes, we examined the association of sleep attentional bias with chronotype, social jetlagand habitual alarm clock usage.

6.2 Methods

Participants

We employed purposive sampling to recruit 155 (70% females) participants between the age range of 20- 35 years (mean age- 23.07, standard deviation- 3.77). Exclusion criteria were the presence of a significant medical or psychiatric history or a diagnosed sleep disorder. All participants were either under-graduate or post graduate students and provided informed consent. Ethical approval for the study was given by the Research Ethics Committee of Maynooth University.

Psychometrics

All participants completed an on-line questionnaire delivered through the Qualtrics platform. This questionnaire including questions relating to standard demographics such as age and gender. The presence of ADHD symptoms was assessed with the *Adult ADHD Self Rating Scale* (ASRS v 1.1), an 18 item self-report sceener where a subject responds to a particular statement by selecting one of the 5 response options ranging from 'never', 'rarely', 'sometimes', 'often' and 'very often' (Adler et al, 2006). The Symptom Checklist is an instrument consisting of the eighteen DSM-IV-TR criteria. To produce a DSM-5 score from the ASRS, the 6 items from the Adult ADHD Self-Report Screening Scale for DSM-5 (ASRS-5) were also included in the measure. Two sets of scores for inattention and hyperactivity/impulsivity were derived from the ASRS 18 items in part A and part B. These scores were then divided into three categories, scores ranging from 0-16 (low ADHD inattention/hyperactivity), scores ranging from 17-23 (moderate ADHD inattention/hyperactivity and scores ranging 24 or above (high ADHD inattention/hyperactivity). Finally, a ADHD consistency/inconsistency category was evaluated from the ASRS v 1.1. The ASRS is described as having a negative predictive value for

clinically-determined diagnosis of adult ADHD of 1 and a positive predictive value of 0.52 (Hines et al, 2012). As such, the screener has very strong properties for ruling out the presence of adult ADHD, and considerably more moderate properties for predicting the presence of adult ADHD.

Subjective sleep quality was assessed through two instruments. The *Sleep Condition Indicator* (SCI) is an eight-item rating scale that was developed to screen for insomnia disorder based on DSM-5 criteria (Espie et al, 2014). A total score of less than 16 indicated probability of insomnia features for the participant. The SCI has been reported to have a predictive value of ~0.85 for clinically diagnosed insomnia disorder according to DSM5 criteria (Wong et al, 2017).

The *Pittsburgh Sleep Quality Index (PSQI)* is a self-rated questionnaire which assesses sleep quality and disturbances over a 1-month time interval (Buysee et al, 1981). Nineteen individual items generate seven "component" scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The sum of scores for these seven components yields one global score. Global scores of less than five indicates good sleeper status, scores of equal or greater than 5 indicates bad sleeper status.

Trait impulsivity was assessed using the *Barratt Impulsiveness Scale* (BIS-11; Patton et al., 1995) in three domains: "attentional impulsiveness", "motor impulsiveness", and "non-planning impulsiveness" as well as a total score . The scale is a self-reported measure consisting of 30 items. Agreement with each statement is endorsed on a four-point Likert type scale ranging from 'Rarely/Never' to 'Almost Always/Always'.

Chronotype and social jetlag were derived from the *Munich Chronotype Questionnaire* (MCTQ; Roenneberg et al, 2003; 2012). This instrument enquires about habitual sleep habits

and timing over the past 4 weeks on "work" days (those with scheduled commitments) and "free" days (those without formal work, study or other commitments). Alarm clock use on "work" and "free" days is asked about in a yes/no question. The key output is the time of mid-sleep (halfway between sleep onset and offset) on work (MSW) and work-free days (MSF). Sleep-corrected MSF (MSFsc) was used to estimate chronotype, to remove compensatory sleep due to accumulated sleep debt (Roenneberg et al, 2012). Social jetlag was calculated as the absolute difference between MSW and MSF, not corrected for sleep debt (Roenneberg et al, 2012).

Sleep Attentional Biases

To assess sleep attentional biases we used custom computerized sleep-related emotional Stroop task, presented via the Inquisit software system (Millisecond, Seattle, USA). Written words were randomly presented individually in the centre of the 15.5-inch computer screen in one of the following keys representing the colours: red (D), blue (F), green (J) and yellow (K). Coloured keys on the computer keyboard were used to record responses. Participants were instructed to place their index and middle fingers over the keys and to press the correct key on the computer keyboard corresponding to the colour of the word on screen as quickly as possible. A fixation cross was presented for 500 ms prior to the word stimuli and between each word. The words were displayed on screen until a response was made. Participants were first given 24 practice trials using words 'one'- 'ten' as practice stimuli, followed by 2 blocks of 160 experimental trials (containing 4 categories of 10 words each, presented with 4 repetitions in random order). The 2 blocks of 160 trials were spaced in between one 2-minute rest period. Word lists contained 10 sleep-related (Barclay and Ellis, 2013), 10 neutral 10 positive words and 10 negative words (as per Bauer and Cox, 1998). The sleep-related words were chosen specifically to be void of any affective connotations. As previous research has demonstrated that participants with ADHD features are more susceptible to higher distractibility when faced

with negative valenced emotional stimuli (such as threat words) in an emotional attention task (Vetter et al., 2018), we did not use the exact test used by Barclay and Ellis (2013) in that we omitted the block of non-specific threat words. The readings obtained from this test included the reaction times for the sleep, negative, positive and neutral words, the interference index which was the difference between the neutral and the sleep/negative/positive word reaction times. Only reaction times from correct trials were included in the analysis; reaction times from error trials were excluded from analysis. We used the sleep interference score (Mean RT Sleep – Mean RT Neutral per participant) as the principal measure of sleep attentional bias, with greater scores indicating more sleep attentional biases.

The study protocol straddled the introduction of Covid-19 pandemic restrictions on Spring 2020. Prior to the introduction of restrictions, the emotional Stroop task was conducted at a desktop PC in a sound proof cubicle (47% of participants). After the introduction of Covid-19 lockdown restriction, the Stroop tasks was delivered on the internet using the Inquisit platform. Analysis of the mode of delivery revealed no difference between the two conditions; for example, comparing the sleep interference scores revealed a P=0.99. As such, data from both conditions was collapsed and treated as one data set.

Data Analysis

Statistical analysis was conducted on SPSS version 26 (IBM 2019). All data was assessed for normality and presence of outliers using the Shapiro Wilk test and histograms. Legitimate values which were noted as outliers through the Box blots were winsorized to 1+the highest value in that distribution and absolute outliers were removed from data set. Groupwise comparison of data was conducted using t-tests or ANOVAs for the primary measure of sleep bias, and MANOVA, for reaction times. Further, reaction time data from the Stroop tasks was assessed via mixed between-within group ANOVAs, with word type (neutral, positive,

negative, sleep) as the within-subject factor and ADHD grouping of insomnia grouping as the between-subjects factor. Correlation analysis was conducted with Spearman's rho. To account for multiple correlation testing in inferential tests, alpha was adjusted to 0.01 for the primary outcome of interest, the sleep bias scores. Reaction time data was treated as secondary outcomes, and alpha was not adjusted from 0.05 for statistical significance.

6.3 Results

29% of study participants were male, and the average age of participants was 23.05 years old (Table 6.1). 36% of participants were identified as being consistent with ADHD from their ASRS scores, and 33% of participants were identified as probable for insomnia disorder from the SCI. 15% of participants scores as being both ADHD consistent and insomnia probably. According to PSQI scores, 81% of participants scored 5 or greater indicating being a bad sleeper. 46% of participants reported habitually using an alarm clock on work-free days and 97% of participants reported using an alarm clock on "work" day mornings. The average timing of midsleep on free days (sleep corrected) was 05:06 and the mean social jetlag was 78 minutes (Table 6.1). ASRS scores were found to correlate moderately with SCI and PSQI scores (more ADHD symptoms associating with poorer sleep), and with MSFsc (later midsleep associating with greater ADHD scores; Table 6.2).

Table 6.1 *Descriptive statistics for the study sample, including performance metrics on the emotional Stroop task and summary scores for the psychometric instruments used. N=155 for the total sample.*

	AGE (years)	RT-SLEEP (ms)	RT-NEGATIVE (ms)	RT-NEUTRAL (ms)	RT-POSITIVE (ms)	ASRS	BIS	SCI	PSQI	MSFsc (hh:mm)	SJL (min)
Mean	23.053	650.062	650.588	650.533	653.395	9.483	63.258	19.703	7.671	05:06	78.071
S.D.	3.793	84.290	85.189	81.007	88.597	3.590	11.090	6.622	3.150	01:13	46.486
Minimum	20.000	415.362	443.887	444.902	473.909	2.000	34.000	3.000	1.000	02:25	0.000
Maximum	35.000	918.771	892.190	911.742	948.760	20.000	101.000	31.000	15.000	08:54	300.000

Note. Ms = milli seconds, RT sleep = Reaction time for positive words, RT negative = Reaction time for negative words, RT neutral = Reaction time for neutral words, RT positive = Reaction time for positive words. ASRS = ADHD rating scale total score, BIS = Barrett Impulsivity Scale total, SCI = Sleep Conditions Indicator total, PSQI = Pittsburg Sleep Quality Scale, MSFsc = Mid Sleep on free days (Chronotype), SJL = Social Jetlag

Table 6.2 *Spearman rho correlation analysis showing associations of the psychometric measures of ADHD symptoms (ASRS), trait impulsivity (BIS), insomnia symptoms (SCI), sleep quality (PSQI), chronotype (MSFsc) and social jetlag (SJL). *** denotes P<0.001.*

	ASRS	**BIS**	**SCI**	**PSQI**	**MSFsc**
BIS	0.513***				
SCI	-0.306***	-0.398***			
PSQI	0.365***	0.390***	-0.702***		
MSFsc	0.277***	0.302***	-0.268***	0.368***	
SJL	0.040	-0.019	-0.142	0.089	0.334***

When examined according to ADHD-consistency (inconsistent/consistent), there was no statistically significant difference in the sleep bias scores on the Stroop test (-3.25±3.41ms inconsistent vs 0.79±3.2ms for consistent, P=0.433; Figure 6.1A). MANOVA revealed no effect of ADHD consistency on RT for any word type (Wilk's Lambda, P=0.648; Figure 6.1 B-E). Further, mixed-between ANOVAs revealed no interaction between word-type x ADHD consistency on RT ($F(3,435)=0.172$, P=0.92; Figure 6.1 F).

When performance on the Stroop task was examined according to insomnia disorder probability status (not probable/probable), there was no statistically significant difference on the sleep bias scores (0.77±0.29ms improbable vs -5.85+4.42ms for probable insomnia, P=0.2; Figure 6.2 A). MANOVA revealed no effect of insomnia probability on RT for any word type (Wilk's Lambda, P=0.11; Figure 6.2 B-E), and mixed-between ANOVAs revealed no interaction between word-type x insomnia probability on RT ($F (3,435) =2.04$, P=0.11; Figure 6.2 F). Further, no effects of PSQI good/bad sleeper status was found on any of the Stroop task scores examined (e.g. sleep bias score -1.57±5.84ms for good sleepers vs. -1.37±2.71ms for bad sleepers, P=0.98).

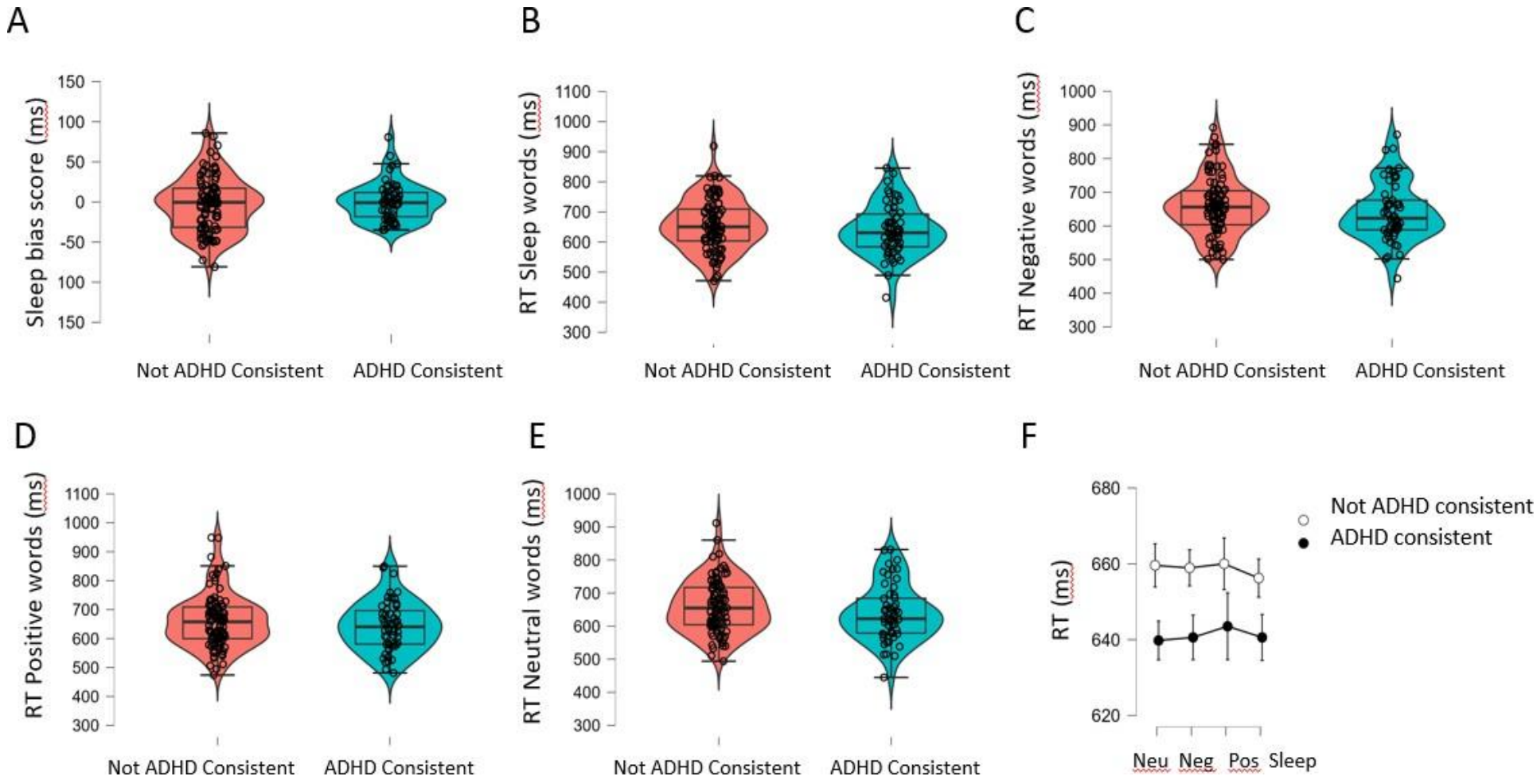


Figure 6.1 *Violin-and-box plots showing (A) sleep attention bias scores (interference scores for sleep words) among ADHD and not-ADHD consistent groups, and ADHD consistency based groupwise comparison of reaction times for (B) sleep-related words, (C) negative words, (D) positive words and (E) neutral words. (F) Line graphs illustratingword-type x ADHD consistency analysis for reaction times (error bars indicate SEM).*

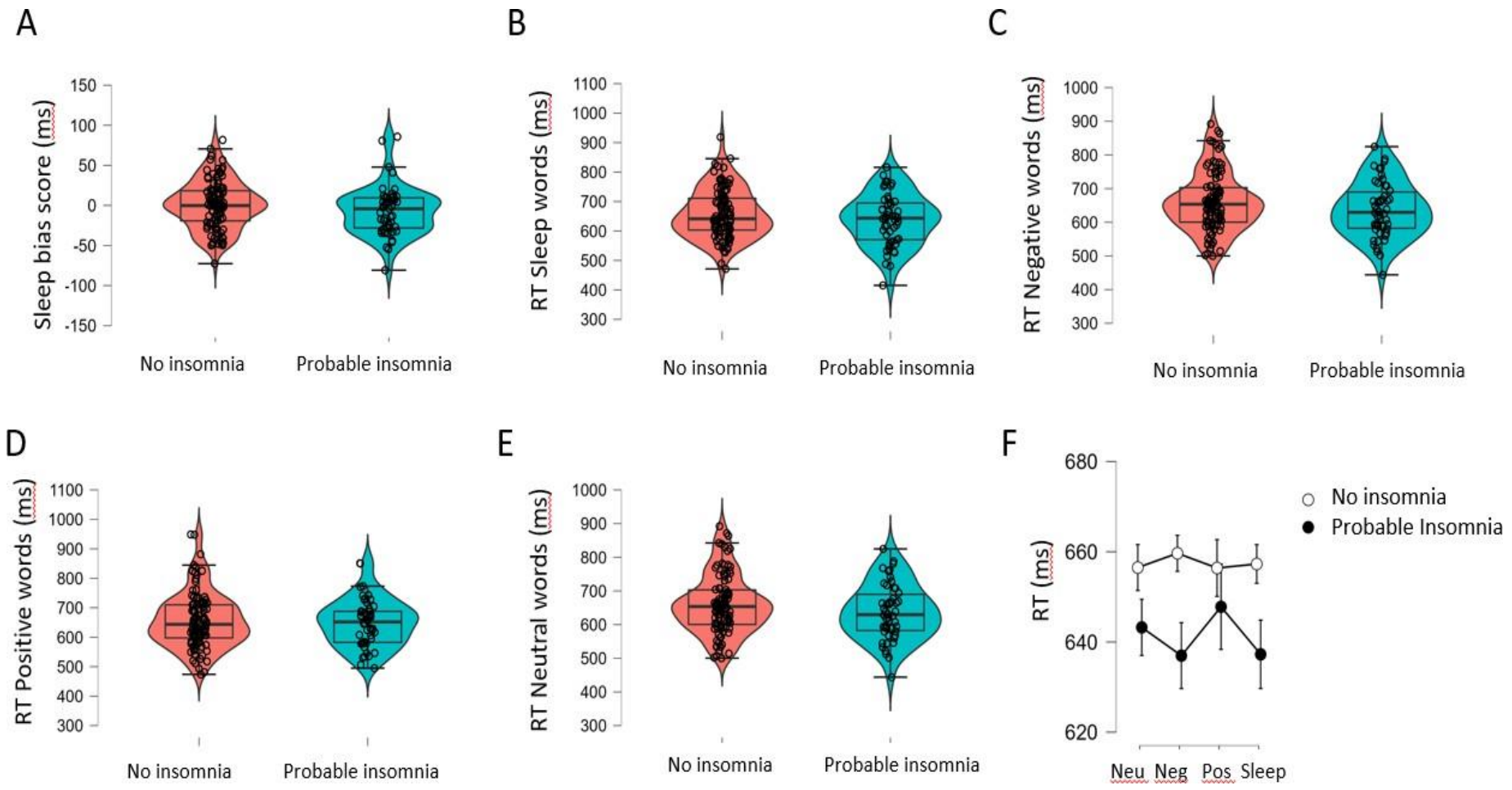


Figure 6.2 *Violin-and-box plots showing (A) sleep attention bias scores (interference scores for sleep words) among insomnia probable and improbable groups, and insomnia probability based groupwise comparison of reaction times to (B) sleep-related words, (C) negative words, (D) positive words and (E) neutral words. (F) Line graph sillustrating word-type x insomnia probability analysis for reaction times (error bars indicate SEM).*

For further analysis, ASRS scores were used to categorise participants according to inattention and hyperactivity/impulsivity status (low/moderate/high) and groupwise analysis on sleep bias scores was examined: there was no effect of either inattention status ($F(2,148) = 1.21$, $P=0.30$; Figure 6.3 A) or hyperactivity/impulsivity status ($F(2,148)=0.61$, $P=0.55$; Figure 6.3 B). We then examined sleep bias scores in individuals who were neither ADHD-consistent or insomnia probable, who were either ADHD-consistent or insomnia probable, and those who were both ADHD-consistent and insomnia probable; there was no effect of combined ADHD/insomnia status on sleep bias scores ($F(2,148) = 0.31$, $P=0.74$; Figure 6.3 C). When examining reaction times for different word types, there was an effect of inattention category ($F(1,144) = 4.82$, $P=0.005$) but no effect of word type ($P=0.541$) or word type x inattention interaction ($P=0.723$; Figure 6.3 D). There were no statistically significant effects ($P>0.2$ for all effect) for 2 way mixed ANOVAs for word type x either hyperactivity category (Figure 6.3 E) or combined ADHD/insomnia category (Figure 6.3 F).

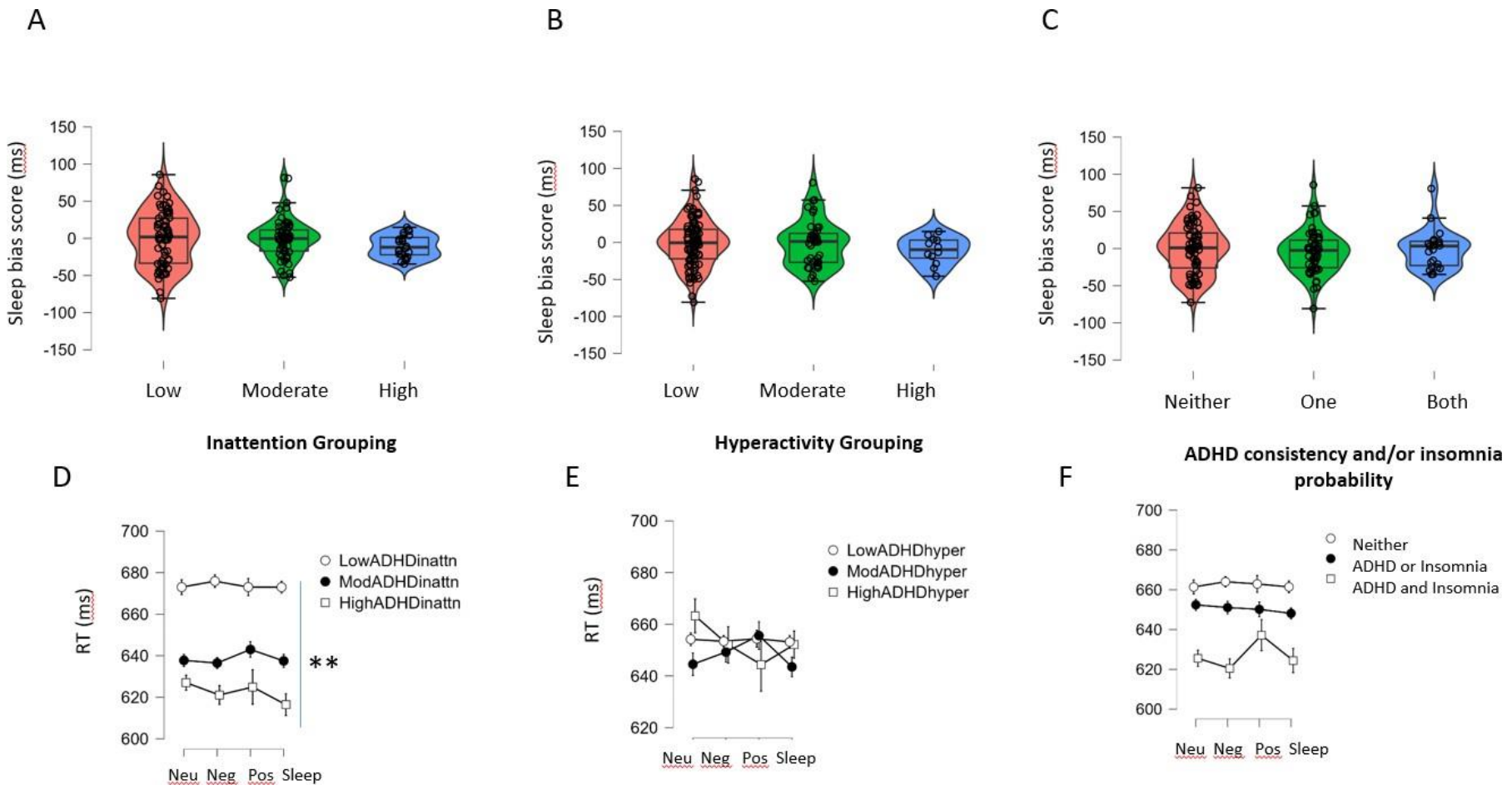


*Figure 6.3 Violin and box plots showing groupwise comparisons for sleep attentional bias scores based on participant classification from the ASRS inattention items (A) , hyperacitivity items (B) and according to whether participants were scored as both insomnia probable and ADHD-consistent, either insomnia probable or ADHD-consistent or neither (C). (D-F) show the analysis of group) x word type effects on reaction times (membership (inattentive group –D; hyperactivity group – E; combined insomnia/ADHD group – F). ** indicates P<0.01 for between group main effect.*

We then examined scores as continuous indicators, and consistent with the above we did not find statistically significant correlations of sleep bias scores with ASRS total score, ASRS inattention score, ASRS hyperactivity/impulsivity score or BIS score for trait impulsivity (Figure 6. 4 A-D). Further, sleep bias scores did not associate significantly with SCI or PSQI total scores, or with MSFsc or social jetlag (Figure 6.4 E-H).

Finally, we explored the association of sleep bias scores with self-reported alarm clock usage on work-free days. Participants who reported using an alarm clock to wake on work-free days showed more sleep attentional bias than those who did not (5.98$\pm$4.1ms for alarm clock users vs. -8.93$\pm$2.98ms, P=0.005) (Figure 6.5 A). Reaction times to sleep (Figure 6.5 B), neutral (Figure 6.5 C), positive and neutral words did not vary according to alarm clock use (P=0.35, 0.93, 0.81, 0.73 respectively). Alarm clock on work-free days use did not vary according to insomnia probability status (P=0.30, chi square test for independence), nor did it vary according to ADHD-consistency (P=0.97). Alarm clock use on work days was not examined as 97% of participants reported using an alarm clock for wakening on work days.

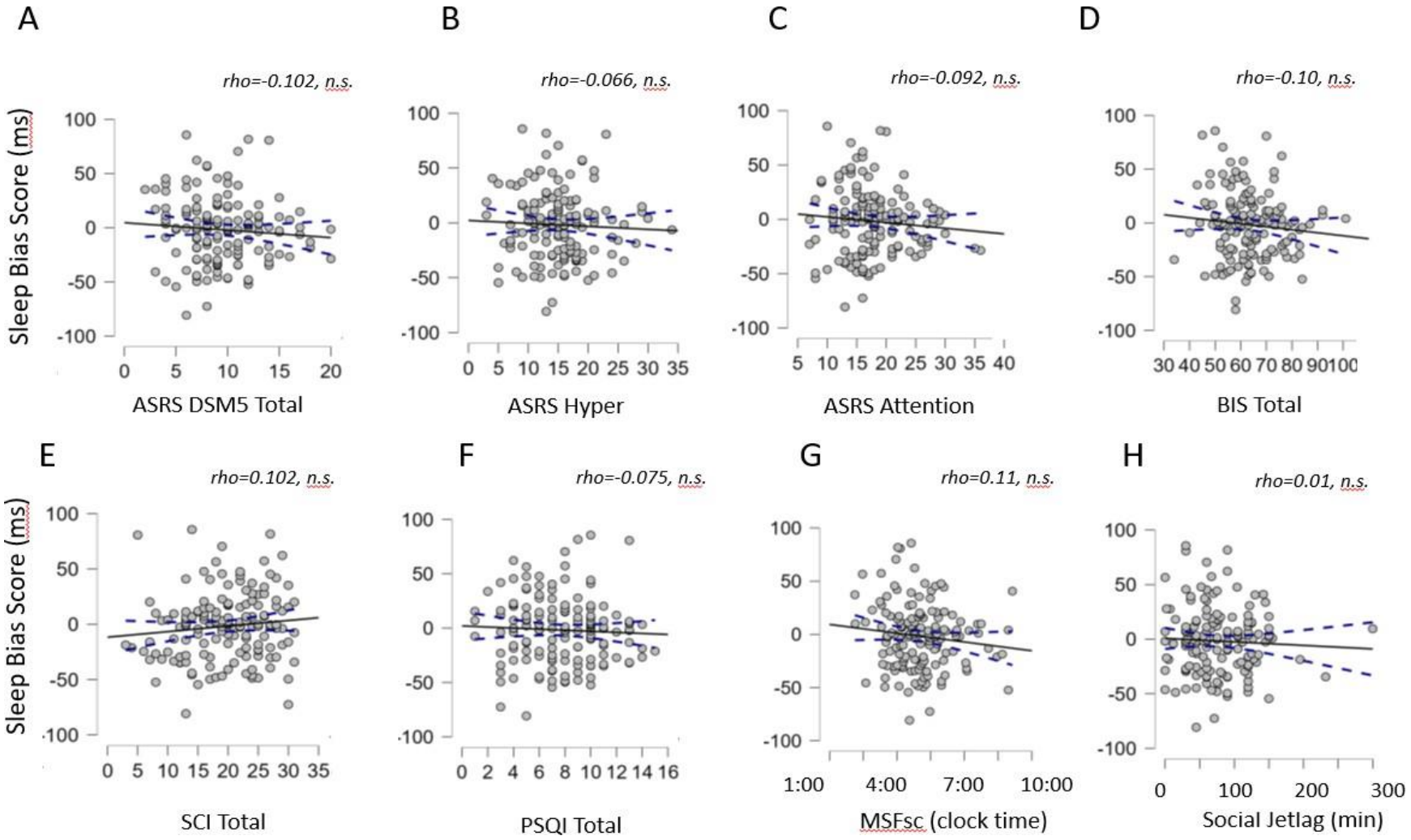


Figure 6.4 *Scatter plots showing the associations of sleep attentional bias scores with (A) ASRS DSM-V scores, (B) ASRS hyperactivity score, (C) ASRS inattention score, (D) SCI total score, (E) PSQI total score, (F) MSFsc and (G) SJL. n.s. indicates non statistical significance via Spearman rho analysis.*

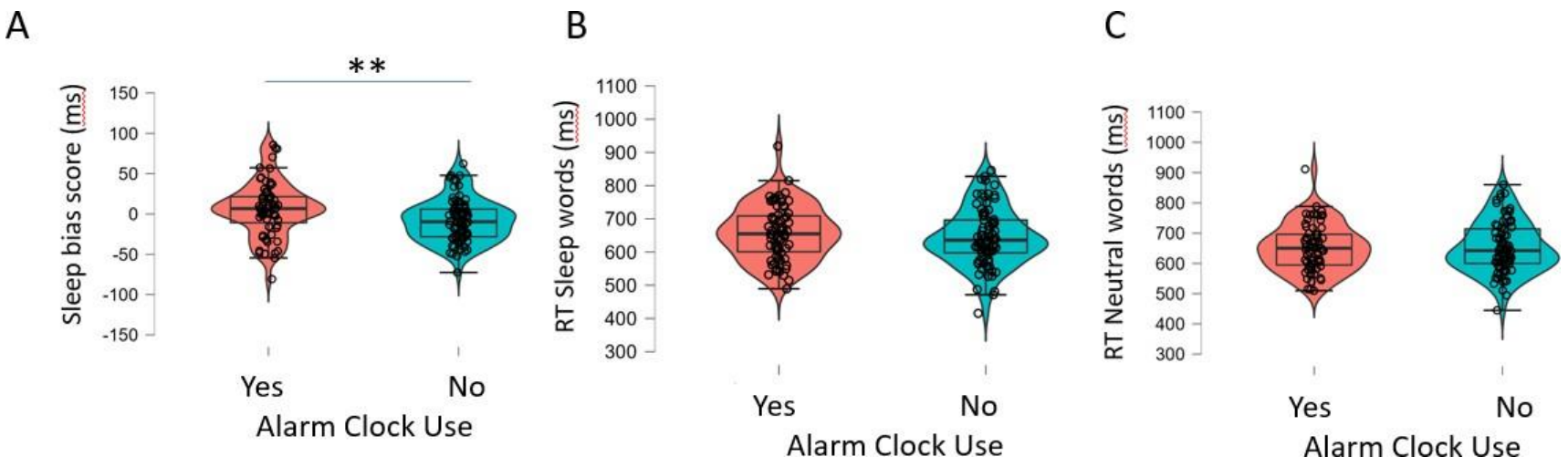


Figure 6.5 *Violin-and-box plots showing groupwise comparisons of (A) sleep attentional bias scores, (B) reaction time to sleep-related words and (C) reaction times to neutral words according to if participant self-reported as habitually using an alarm clock on work free days. ** denotes P<0.01 by independent samples t-test.*

6.4 Discussion

In this study we examined whether subjectively reported ADHD symptoms associates with sleep attentional bias, assessed with a sleep Stroop test. Further, we examined whether insomnia symptoms and sleep quality also associated with sleep attentional bias, as well as examining the associations of sleep attentional bias with chronotype, social jetlag and habitual alarm clock use. We did not find any association between ADHD-consistency and insomnia probability on sleep bias scores, nor did we find an effect of combined ADHD-consistency and insomnia probability. We did find that habitual alarm clock use was associated with greater sleep attentional bias.

Previous research has inconsistently reported the presence of attentional bias in insomnia disorder, although cognitive models of insomnia includes bias to sleep related stimuli as a component features (Akram et al, 2022; Harris et al, 2015). Given that sleep problems are commonly reported in adults with ADHD (eg. Coogan and McGowan, 2017), we hypothesised that ADHD features would associate with sleep attentional bias. We were somewhat surprised that neither ADHD nor insomnia features associated with sleep attentional bias, as previous literature has indicated that insomnia and having poor quality sleep was associated with sleep attentional biases, as indicated by various tasks to assess the bias (Taylor et al 2003; Jones, et al 2005; Macmohan, et al 2006; Barclay & Ellis 2013). Whilst some previous studies used reaction times to sleep-related words on the emotional Stroop test as an indicator of sleep attentional bias, rather than the sleep bias score based on the sleep word interference score (eg. Barclay and Ellis, 2013), a recent meta-analysis has recalculated those values as sleep bias scores and report that sleep attentional biases are indeed associated with poor sleeper status and with the presence of insomnia disorder (Akram et al, 2022). Further, we did not detect any groupwise differences on reaction times for sleep-related words according to either ADHD-consistency or insomnia probability; as such, we do not believe that the lack of associations

detected is contingent on the measure used (sleep bias score vs. reaction time for sleep words). It is notable that a number of previous studies did not report an attentional bas towards sleep-related stimuli in individuals with insomnia (Lancee et al., 2017; Lundh et al., 1997; Speigelhalder et al 2008; & Clarke et al., 2016). One reason for discrepancy in the literature is the nature of the task that is used to assess this attention bias and the nature of the sleep related stimulus presented to the participant, with the emotional Stroop test reported to be less sensitive to sleep attentional bias compared to dot-probe, flicker or Posner tasks (Harris et al. 2015). Fabbri et al (2022) used the Dot-Probe to suggest that insomnia is indeed related to greater difficulty in switching from sleep related stimuli. However, the emotional Stroop test is more likely to represent the influence of heightened arousal that might interfere with the processing of sleep- related visual stimuli (MacMohan et al 2006; Marchetti et al 2006).

One consideration is that the study of Barclay and Ellis (2013), which did use an emotional Stroop task, sampled participants in the evening time (rather than the day-time in the current study); as such, greater homeostatic sleep pressure associated with later in the day may contribute to the detection of sleep attentional bias. A final consideration is that in our study, sleep quality and the probable insomnia status was determined by subjective measures, rather than objective tests such as actigraphy or polysomnography. Spiegelhalder et al. (2010) demonstrated an unexpected positive association between attention bias and improved markers of sleep duration and continuity measured by polysomnography when using a Dot probe task, however attention bias on the emotional Stroop task was not correlated with the polysomnography parameters.

Inattention category was associated with a main effect on reaction times that was not sensitive to word type, with those with lower levels of inattention showing slower reaction times to all word types. Hyperactivity category was not associated a main effect on reaction times, and neither inattention or hyperactivity category was associated with sleep bias scores.

Shushakova et al (2018) reported that participants with ADHD tended towards slower reaction times towards emotional words; however, our results indicates that reaction times are similarly slower to neutral, positive, negative and sleep-related words in participants with low inattention. Posner et al (2011) showed differences in reaction times were slowed by positive and negative distractor words in healthy control, and people with ADHD. The most straightforward explanation of the current finding is that participants with low inattention will be most prone to cognitive distraction of the interfering words on the Stroop task, and as such will display slower reaction times independent of word type (hence the lack of bias scores as reaction to neutral words are similarly slowed as test words). As sleep problems are associated with increased inattention (eg. McGowan et al, 2021), we suggest that future work on assessing sleep attentional biases in poor sleep and in sleep disorders should incorporate indicators of general inattention.

We did find a sleep attentional bias in participants who habitually used alarm clocks to wake on "work-free" days versus those who did not, indicating that participants whose sleep on work free days was curtailed by their social demands were more cognitively oriented towards sleep- related stimuli (no bias effect was detected for positive or negative words). Especially for the student population, whose 'workdays' might not be so straightforwardly demarcated from 'work free' or weekend days (due to part time jobs, engagements with friends and family and personal tasks). Interestingly there was no relationship of social jetlag to sleep bias, indicating that alarm clock use in this contextappears not to be a proxy for social jetlag. Interestingly, a recent report has identified the Munich Chronotype Questionnaire as the only sleep questionnaire that asks about the method of wakening (Robbins et al, 2021). As such, alarm clock usage, or other methods of wakening, may be underexplored factors in exploring cognitive processes in sleep disorders. Clock monitoring has been proposed as a factor that contributes to the persistence of insomnia disorder through amplification of pre-

sleep worry (Tang et al, 2007), although it is not clear if habitual alarm clock use may influence clock monitoring behaviours. It is also not clear from the current data which, if any, other wakening method participants (who did not use alarm clocks) utilized to facilitate wakening both on free and work days. This can be considered a limitation of the present study, that future studies can take into account.

There are a number of important limitations in our study. Participant's sleep measures were based on subjective reports rather than a combination of objective and subjective tools, thereby not controlling for personal biases in responses and the effect of individual differences in interpretation of inventory questions. ADHD features were evaluated through a screener questionnaire rather than a comprehensive diagnostic assessment tool, introducing the potential for confounding effects arising from participants' misinterpretation of item questions. Further, we did not explore the participant's psychological/mood states which might have affected their performance on the Stroop test and even on the questionnaire, nor did we assess acute sleepiness at the time of testing. The Stroop test employed was custom modified, with the sleep words from the Barclay and Ellis (2013) study added to previously used alcohol Stroop test by replacing the alcohol words with the sleep words (Bauer and Cox 1997). Participants were young adult university students, and as such findings might not generalise to other populations. Finally, the effect of alarm clock use on sleep attention bias was discovered during exploratory analysis and was not tested as an *a priori* hypothesis.

Conclusion

The aetiology of sleep problems commonly reported in ADHD remains poorly understood. The examination of cognitive factors implicated in insomnia and other sleep disorders in sleep problems in ADHD will be of importance, given the cognitive nature of the core symptoms of ADHD. The current findings do not implicate sleep attentional bias as part of link between ADHD and sleep, although as noted there are doubts in the literature as to

whether sleep attentional biases play substantive roles in insomnia.

Chapter 7: General Discussion

Recapitulating sleep in childhood ADHD and the need for future research

7.1 The Beginning

Research on ADHD and sleep has intensified rapidly in the last couple of decades, with the preliminary investigation (Bergman, 1976) focussing on behaviour therapy as an intervention for childhood insomnia and physiological examination of sleep in children with hyperkinetic disorder showing changes in REM sleep duration and movement during sleep (Busby et al 1981). Until the early 1990s, sleep disturbances in childhood ADHD was seen mostly in the context of hyperactivity (Busby and Pivik, 1985; Chatoor et al 1983; Kaplan et al 1987; Greenhill et al 1983). This was evident from its inclusion within the hyperactivity domain for the diagnostic criteria of Attention Deficit Disorder ('Moves about excessively in sleep') in the Diagnostic and Statistical Manual of Mental Disorders (3rd edition) (American Psychiatric Association, 1980). For children with ADHD worse sleep has consistently been indicated both in investigations through objective (actigraphy, multiple sleep latency test and polysomnography recordings) and subjective (parent/self-rated questionnaires or sleep diary) methods over the decades as discussed in some seminal reviews (Cortese et al 2009; Spruyt and Gozal 2011; Martins et al 2019; Becker et al 2020; Sciberras, 2022).

The type of sleep problems in this population span from sleep onset difficulties (delay falling asleep, anxiety regarding sleep, emotional and behavioural regulation concerns) (Mindell and Owens, 2015; Lecendreux and Cortese, 2007;Weiss et al 2006) and overnight sleep concerns (nocturnal awakenings, restless sleep, nightmares, sleep related breathing concerns, snoring) (Cortese et al 2008; Chervin et al 2002; Konofal et al 2001), to difficulty waking up in the morning, prolonged tiredness upon waking, and excessive daytime sleepiness (Sung et al 2008; Owens et al 2009). Actigraphy-recorded macrostructural sleep properties among children with ADHD demonstrated shorter sleep duration, longer sleep onset latency; increased sleep fragmentation and WASO duration (Wake after sleep onset) (Lee et al 2014; Miano et al 2019; Shrivastava et al 2014), whereas PSG/MSLT-recorded microstructural sleep

properties found shorter REM sleep, lower duration of total Non-REM sleep and stage 2 (N2) sleep, less mature topographical distribution of Slow Wave Activity (SWA) in the sub cortical regions of the brain and greater Apnea-Hypoapnea Index (Akinci et al 2015; Grissom et al 2009; Ringli et al 2013; Miano et al 2019).

7.2 Impressions from this Thesis

In our research project, a systematic review of the extant literature revealed that the above findings are not ubiquitous in all study cohorts, which could be attributed to the lack of comprehensive and multifaceted assessment of sleep (using both objective and subjective tools), comparatively fewer ADHD subtype based analysis of sleep difficulties, less studies distinguishing ADHD specific sleep problems from the transdiagnostic presentation of sleep difficulties, and the need for longitudinal studies examining temporal development of sleep problems in this population (Bondopadhyay et al 2022). Moreover, most of the research has been cross sectional in nature and have not examined brain substrates or mechanisms (Shen et al 2020). At a neuroanatomical level, ADHD is associated with structural abnormalities and variabilities in corticostratial circuitry, which has also been identified in sleep disturbances such as insomnia (Hoogman et al 2017; Atena et al 2010; Stoffers et al 2013). Common abnormalities in the frontostriatal and salience/ventral attention networks has been indicated both in sleep problems as well as ADHD, although not yet examined (Hegerl and Hensch, 2014; Owens, 2005). Additionally, at a molecular level, both dopamine (Volkow et al 2009) and norepinephrine (Arns et al 2000) neurotransmitter system dysregulations play a role in ADHD symptomatology and sleep regulation (Biederman and Spencer, 1999). Therefore, when investigating sleep disturbances and ADHD symptoms, acknowledging the underlying overlapping pathophysiology might be helpful. That is to say, rather than drawing relationships between the two conditions or asking which came first, future research should explore the impact of this relationship and how it can be altered.

Studies with younger cohorts have revealed that infants with familial risk for ADHD have less stable sleep (Landau et al 2010). Moreover, some sleep problems may develop particularly in the context of ADHD symptomatology, for example, behavioural sleep-based problems (insufficient limit setting by parents, sleep hygiene concerns and counterproductive conditioned behaviours for sleep onset), physiological sleep variabilities (nocturnal awakenings, daytime sleepiness or chronic sleep onset insomnia), or the use of ADHD medications (for example stimulants) (Weiss and Salpekar, 2010). Sleep problems was also related with poorer quality of life and daily functioning, heightened behavioural problems, worsened cognitive and executive functioning, less punctuality for school among these children (Sung et al 2008; Craig et al 2020; Lambek et al 2021; Loram et al 2021). Additionally, worse outcomes for parental sleep and mental health (Buxton et al 2015; Martin et al 2019) and lower occupational productivity (Sung et al 2008) was indicated as a result of sleep disturbances in children with ADHD. Therefore, exploring beyond group differences in sleep problems and moving towards questions like how sleep problems develop in childhood ADHD, what are the risk factors for these difficulties and their dominant functional outcomes would be an important next step considering detailed facets of developmental psychopathology (Becker et al 2020).

Building Blocks of Sleep within the ADHD Clinical Picture

We revert to Frank, the 9-year-old boy mentioned in our prologue. Frank presented academic and behavioural concerns especially in the school and home settings, demonstrating lack of selective attention and behavioural inhibition. The findings of a psychological assessment warranted the diagnosis of ADHD (combined presentation), however on probing about his day-to-day functional problems, major difficulty with Frank's sleep wake patterns came to light. Frank slept by midnight on school nights, preferred completing his homework late at night before sleep, had major difficulty waking in the morning on time for school, missed

breakfast as he has to get ready for school in haste, was reported to become irritable after lunchtime and was likely to get into fights with schoolmates during class dispersal.

We will recapitulate the major findings from our empirical studies to conceptualise developmental psychopathology pathways that may have solidified Frank's sleep problems. Proceeding from our systematic review, we recognised the abundance of quantitative studies employing subjective questionnaires. However, caregiver rated questionnaires might be vulnerable to respondent related or psycho-social or environmental biases (Sciberras et al 2016, 2017). As a result, we embarked upon a qualitative investigation of sleep in childhood ADHD, which allowed for more granular and contextual richness in the information collected, and created a nuanced framework for understanding parent perceived sleep problems in their children with ADHD. Our study included the thematic analysis of 26 semi-structured interviews with parents of preadolescent children diagnosed with ADHD. We found that parent's perceived sleep for their children revolved around the child's sleep difficulties (including difficulty initiating sleep, emotional distress affecting sleep, waking early despite late sleep onset); the impact of these sleep problems (including behavioural problems/emotional outbursts, influence of on parents' sleep/evening schedule, sleep problems as a motivation for ADHD assessment); and steps taken by parents to improve children's sleep (activities/behaviours encouraged before bedtime, medication effects on children's sleep, active steps to improve children's emotional state to help sleep and use of items/accessories and bedroom features to help sleep).

Executive Dysfunction and Sleep Initiation

Re-visiting Frank's difficulty in falling asleep and preferring to complete school tasks during the latter part of night echoed the above trends we pointed in our results. Executive dysfunction has previously been linked with sleep problems for children in this population

(Becker et al 2016) and this relationship could also be described as bidirectional in nature, for example sleep deprivation associated with greater cognitive and emotional dysregulation (Nilsson et al 2005; Cohen et al 2016; Floros et al 2021). Our data suggests that poor executive control contributes to children's poor communication, planning and winding down in the hours prior to bedtime. Brown (2008) described functional impairments in ADHD resulting from 5 components:

1. Poor 'activation' skills which includes facets such as organizing, prioritizing, estimating time and starting on a task (in case of sleep, this could mean child not being able to efficiently complete his pre-bedtime activities without supervision).
2. Poor 'focus' which includes facets such sustaining, shifting and paying attention; difficulty with 'effort' which includes tasks such regulating alertness, effort to continue with a task and processing speed (for sleep this could mean transitioning from a non-sleep related activity to getting ready for bed, difficulty completing pre-bed routines).
3. Difficulty in managing frustrating and modulating 'emotions' (when the child is unable to wind down to sleep as a previous/ current emotional problem is having an interfering influence);
4. Poor memory skills in areas of working memory and accessing recall (child unable to follow multistep instructions or retain how their caregiver helped them get ready for bed the previous night for example); and
5. poor 'action' skills which includes self-monitoring and self-regulation skills (with regard to sleep, this could impact the child by him getting distracted while completing his night time chores, going in to the day dreaming mode while completing a task, or starting another incomplete task while getting ready for bed).

Frank preferring tasks at night and getting upset if parents persist could then be attributed to his executive dysregulation.

Impact of Sleep Problems on Waking Difficulties and Morning Behavioural Concerns

Frank did not wake early despite late night sleep onset (a trend we underlined in our qualitative study), and in fact had considerable difficulty waking and alerting himself in the morning. The second largest standardized mean difference was previously found in difficulty with morning awakenings when compared to controls as reported in a meta-analysis (Cortese et al 2009). Spruyt and Gozal (2011) in their review explained that bedtime refusal and daytime somnolence could also result from a delayed endogenous circadian rhythm in these children, however the authors reiterated that lack of parenting consistency in enforcing bedtime schedules, thereby possibly not controlling the executive dysfunction at play, as a possible reason why the child would not go to sleep at a time aligned to their circadian clock. Looking at daytime functional impacts of Frank's sleep problems, for example, excessive daytime sleepiness and behavioural outburst (after lunch break till school dispersal) could be replicating sleep impact details presented by parents in our qualitative study, as also seen in previous studies (Craig and Weiss, 2017; Mayes et al 2009). The only other qualitative study examining sleep in children with ADHD, also reported association between poor sleep and emotional and behavioural difficulties (Harris et al 2022).

Comorbidities and their Roles in Sleep in ADHD

The presence of comorbid conditions characterised by externalising or internalising behavioural problems has previously been associated with higher degree of sleep problems in ADHD children (Cortese et al 2009), thereby calling attention for research studies to shed light on the participant's comorbid psychopathology. Research has indicated behavioural/emotional comorbidities as risk factors for sleep problems (Lycett, et al 2016), and also as a marker for early age occurrence of sleep problems (Sciberras, et al 2016) in this population. One limitation of our empirical investigation (Chapter 4) was that we did not explore the presence of

associated comorbidities, a point to be considered for future research. However, as we employed qualitative analysis (in chapter 3), detailed open ended conversation with the parent resulted in gathering an in-depth account of comorbid conditions and how it interacted with the child's core ADHD symptoms and sleep problems.

Sleep Difficulties and Diagnostic Clarity

Franks' parents highlighted his sleep problems which were part of the symptomatology reported to the psychologist, thereby establishing an equally crucial impact of the core ADHD related difficulties and those related to sleep. An ADHD diagnosis is dependent not only on the reported presence of clinically significant inattention and/or hyperactivity-impulsivity, but also the careful assessment of the number of areas the presenting complaints are impacting (American Psychiatric Association, 2013). This highlights sleep as an important factor, as 25-55% of children with ADHD report sleep problems (Lunsford-Avery et al 2016; Virring et al 2015) which can impact diagnostic formulations as well as establishing differential conditions. As such, the theme of sleep difficulties providing diagnostic clarity was generated in our qualitative analysis. Virring et al (2014) found that although ADHD children reported more sleep problems, sleep problems affected daily functioning regardless of whether the child has an ADHD diagnosis, the extent to which sleep exacerbates functional impairment is still a question that needs careful thought.

Impact of Children's Sleep Problems on Parents and the Household

Our study found that the child's sleep was negatively impacting parent's night time schedules of sleep and other planned activities. Sleep as a family concept drives reciprocal sleep interactions between family members (Buxton et al 2015); that is, children's sleep disturbances affecting parent's sleep and mood; and parental insomnia associating with children's sleep problems (Zhang et al 2010). Children's sleep patterns would develop within

the family context dynamically influenced by the family relationships (El- Sheikh and Kelly, 2017). Frank's parent's although did not report impacts on their family life due to Frank's night routine, during the course of the assessment and subsequent therapeutic interventions, parental role confusion (as seen in Podolski and Nigg, 2001) and difficulty engaging in their own night schedules were highlighted. And this in-turn supposedly solidified specific sleep-wake patterns for Frank and his family over time. Our second empirical study, which explored the relationship between child's sleep and parent insomnia probability and ADHD screener measures (Chapter 4), found that sleep problems in children with ADHD were greatest for those whose parents were both insomnia probable and ADHD consistent based on a screener. Poor sleep in adults has emotional, stress-related and psychiatric consequences (Konjarski et al 2018; Hisler and Krizan, 2017; de Estrela et al 2018) that in turn may affect their parenting behaviours (McQuillan et al 2019) and subsequently affect the child (Bordeleau et al 2012; Johnson et al 2008).

Interventions to Improve Sleep in ADHD: at Home and at the Clinic.

In their review, Becker et al (2020) explained that when considering the relationship between childhood sleep and ADHD symptoms, which have been documented (Corkum et al 2013; Sung et al 2008), the next step would be to establish causal relationships between these variables. Several experimental design studies have also attempted to study the effect of altered sleep patterns on ADHD-specific cognitive functions, such as performance on attentional and executive function tasks (Floros et al 2021; Becker et al 2019; Cremone-Caira et al 2019). Our research project, which explored the environment and its effect on the ADHD child's sleep facets, as well as its bidirectional role, further points towards the need for examining clinical application of the findings in this field, as do other studies (Craig et al 2020; Malkani et al 2022). Our qualitative analysis revealed that parents take steps to improve their child's sleep

concerns through encouraging specific activities before bedtime, using particular items and accessories, trying not to emotionally trigger the child in the hours before bedtime, and use/views on ADHD and sleep medication. We found that parents used storytelling, meditating to help induce calm and make the child wind down to sleep; bargaining, negotiating, sticking to routines to facilitate consistency; and waiting in children's room if their presence calm them down, or restricting screen time or carbonated drinks that might be counter-productive for sleep; and encouraged physical exercise during the day. Individualised strategies to promote sleep in this population has previously been noted (Nikles et al 2020), with need-based parent psychoeducation (Cortese et al 2013), cognitive behavioural interventions (Sciberras et al 2011), using strategies such as relaxation and distress tolerance; and sleep hygiene based interventions (Peppers et al 2016) have further been useful as was also indicated in our analysis.

Weiss et al (2006) conducted a RCT to trial the combination of sleep hygiene routine plus melatonin administration, where parent, child and clinicians designed the sleep timing of the child based on their routine, resulting in decreased sleep onset latency for the children. In the case of Frank, his parents had an established bedtime routine, although later at night than recommended and under constant parental supervision. Upon starting intervention, bedtime routines designed with the psychologist took into consideration Frank's specific areas of executive function deficit; for example, self-regulating and lack of sustained attention, which made it difficult for him to complete his after-dinner school tasks, pre-bed routines and read his storybook in bed. Taking attentional and sensory breaks, chunking and starting individual school tasks right from the afternoon, receiving his screen time before dinner, and replacing the story book with an audio book while Frank plays with a fidget toy on bed proved to be helpful for him.

Considering fidget toys, sensory seeking or variabilities in sensory processing have been reported in ADHD symptomatology (Ghanizadeh, 2011) and these are associated with

sleep problems in children with ADHD (Minouni-Bloch et al 2021). Our qualitative study found parents encouraging their children to engage with sensory calming items (such as play dough, stuffed toys, familiar blankets, particular lighting, child specific optimal temperature, and background sounds) during bedtime to facilitate sleep. A recent study (Hartman et al, 2022) found that children with higher sensory sensitivity had more self-reported and parent- reported sleep problems, as well as had higher frequencies of sleep anxiety, bedtime resistance and sleep onset delay. Sleep and sensory processing in paediatric populations is a topic of recent interest (Rajaei et al 2021) and as such in the ADHD context, future investigations should employ both subjective reports and objective sleep measures to ascertain its relationship with sensory processing variabilities in this population. Although we found parents employing different strategies to facilitate sleep in their children, the source of such information could further be explored in future studies so that readily available comprehensive sleep promoting information platforms can be created for parents that can be accessed through school networks or clinics. This suggestion again echoes the need for a partial paradigm shift of research in this area from correlation and causation-based studies to application-based investigations.

A variety of sleep conditions have shown improvement when treated with appropriate time of day bright light therapy (BLT) (Crowley et al 2004; Revell and Eastman, 2005; Wilhelmsen-Langeland et al 2013; Wilhelmsen-Langeland et al 2014). While early evening light exposure leads to a phase delay (wake time shifts to a later time), early morning light exposure shifts the wake time to an earlier time (phase is advanced) (Klein & Weller, 1970; Tamarkin et al 1979). Although standard pharmacological treatment for ADHD do not target the circadian rhythm delays in these patients, and ADHD symptom severity is associated with delayed sleep timing (Gamble et al 2013), BLT as a treatment approach has not been widely researched in pediatric population. Fargason et al 2017, demonstrated that BLT advanced Dim Light Melatonin Onset (DLMO) and mid sleep time in adults with ADHD. A decrease in ADHD symptoms was also reported. Future research could assess the efficiency of BLT

interventions among younger ADHD diagnosed populations. Such an intervention not only can be assessed suing a objective circadian phase marker (DLMO), but can also demonstrate its effect on the child's core ADHD symptoms, while decreasing their dependence on prescribed stimulants.

Children's Sleep and ADHD Medication

Our quantitative investigations found that a higher percentage of children on medication were reported having a sleep disorder, while our qualitative analysis indicated that medication might have a two-sided effect, bettering the child's daytime functioning, but making it difficult for the child to fall asleep, however reducing night time anxiety helping the child get a deeper uninterrupted sleep. Research focussing on the effect of ADHD medication on sleep mimics similar trends, highlighting both positive and negative impact of medication (Kidwell et al 2015; Tomas- Vila et al 2010). From a clinical perspective sleep problems arising from ADHD medication can take several forms: either sleep timing varies, however sleep efficiency improves, or become more variable; comorbid symptoms and important areas of functioning are improved and as a result sleep also improves; and sleep problems due to medication will result in attempting to achieve an optimal dose or formulation (Stein et al 2012). The course in which sleep problems emerge after medication intake might differ based on formulations (for example, those affecting circadian rhythms might have a more subtle insidious effect and can surface later when the child has already adjusted to the medication, Spruyt and Gozal, 2011). These complicated treatment effects might help longitudinal studies, employing objective measures together with subjective reports (especially those gathering open ended qualitative data) to uncover more information.

Assessment of Sleep

Stein and colleagues (2012) stated the importance of assessing sleep functions before starting treatment for ADHD. Such information should be assessed during the initial diagnostic

assessment and case formulation by the psychologist/ mental health professional. This underlines the importance of training for clinicians about age-appropriate sleep and sleep pathology. Ascertaining information about difficulty winding down to sleep, falling asleep, maintaining sleep, parasomnias, or difficulty waking up in the morning or daytime tiredness, together with antecedents for poor sleep and night to night variability should be the first step. This could be followed by a brief psychoeducation about healthy sleep practices and facilitating sleep in the child by individualised symptom and comorbidity based needs (for example if the child has difficulty regulating emotions, use of a parent maintained thought diary during pre-bed activities, or if the child is overly sensitive to certain bedtime cloth's texture, optimally substituting it with a comfortable fabric). However, in real world clinical settings, there is limited time within which the clinician must ascertain vital information about the child and their environment to reach a provisional case formulation. In such a situation, probing about detailed sleep functions of the child might be difficult and a ADHD specific sleep questionnaire could gather crucial information about the child's sleep. We designed a novel questionnaire to assess sleep in childhood ADHD, CASS (Childhood ADHD Sleep Scale), which focused on ADHD specific sleep problems in the child (for example, executive dysfunction and its role in hampering sleep practices). Although the pilot version of this tool demonstrated good psychometric properties, trial with a larger sample to conduct detailed statistical exploration is a necessary next step.

Frank's management and treatment plan would respond positively to such a thorough investigation of his sleep functions right at the time of the initial clinical assessment. This would be contingent upon the clinician's knowledge base regarding prominent sleep problems and their enablers in the ADHD clinical picture. Additionally their clinical judgement on how the interaction effect of Franks' comorbidities and core ADHD symptomatology with the sleep problems effects his overall functioning, would facilitate the design of an individualised management plan for him and his family. Such a comprehensive treatment plan would

plausibly have a knock-on impact to improve Frank's cognitive, behavioural and emotional regulation, his social skills, academic performance and overall family wellbeing.

7.3 Reflections on Strengths and Weaknesses of the Project

An important strength of this thesis was that we commenced our research project with a systematic review of studies that have explored sleep in childhood ADHD. We did not present the results of our review in the form of a general account of sleep disturbances or only one aspect of sleep in ADHD; rather we presented a comprehensive picture of sleep and circadian rhythms within the ADHD symptomatology, its functional consequences, and extended our investigation to how interventions for ADHD and sleep affects the child's functioning. In doing so, our review acknowledged the subjective reports and objectively measured macro and microstructural sleep properties in ADHD, thereby also underlining the discrepancy in findings for certain sleep problems when using each kind of data collection tool. For example, in subjectively reported sleep functions findings might vary due to parent's overappraisal of sleep problems, inaccurate understanding of the survey questions, lack of questions addressing impact of sleep problems on family members and household, or lack of ADHD subtype-based recruitment, whereas in objective techniques not using optimal actigraphy study protocols, first night effects in studies utilizing polysomnography, possible effects of abstaining from ADHD medication during the study period, and smaller sample sizes might impact the direction of the literature. We underlined how the overall lack of longitudinal studies (accounting for emerging and existent comorbidities in the child's dynamic social environment) and the lack of multisite intervention studies might prove to be an obstacle in establishing a developmental psychopathology based framework of sleep problems for ADHD children.

Responding to the above stipulations, we designed our first empirical study where we used semi structured interviews with parents to assess their child's sleep and analysed the results qualitatively using thematic analysis (Chapter 3). Using a qualitative analysis was an

important strength in the thesis, as this takes into consideration the child's environment, family and parental wellbeing, when discussing their sleep patterns, presenting not only a granular account of these difficulties but also the nature of their longitudinal development. There is only one more qualitative investigation of sleep-in childhood ADHD (Harris et al 2022), however it focusses on parent perceived impact of child's sleep quality on their functioning. We presented our understanding of the generated themes in a holistic format, including the child's sleep problems as perceived by the parents, what they think are its impacts and steps taken to overcome these difficulties. Presenting such a comprehensive account helped us underline novel facets such as the role sleep problems play in seeking clinical attention, or how sleep disorder investigations might lead up to a further detailed neurodevelopmental assessment thereby receiving a ADHD diagnosis (which then explains the functional problems in the child's life).

Additionally, one major strength of our thesis was that it highlighted the role of executive functions in precipitating and perpetuating sleep initiation and sleep routine problems. Although previously sleep problems in this population has been bidirectionally associated with increased executive dysfunctions (Becker, 2020; Floros et al 2021), our project discussed how bedtime routines and sleep initiation can be impacted by executive function deficits in planning, focus, activating, and regulating impulses. Our findings here resulted in a ripple effect understanding of why parents established child's executive function deficit specific steps to facilitate their sleep.

Because our systematic review highlighted the relationship between parental sleep and mental health and child's sleep and further, our qualitative study underlined the specific impact the child's sleep might have on the parents and the household, this further paved the way for us to explore quantitatively whether parental sleep (insomnia probability) and the presence of ADHD symptoms might be associated with child's overall sleep problems. This flow of

investigations focussing on the bidirectional relationship between parent's and child's sleep was a major strength of our thesis. We not only found that children of parents who are both insomnia probable and have (screener based) features of ADHD have more sleep problems as compared to children whose parents had either or none (highlighting the double impact), but also underlined how child's sleep initiation and maintenance problems impact parent's functioning (night time schedule and their own sleep).

Another important strength of our thesis is that through a thorough review of the existent literature, a detailed qualitative study and a quantitative investigation, it proposed a plausible route through which an ADHD child and their parent's sleep and mental health might be associated (regardless of directionality). One route of this association is that as adults with ADHD who are known to have sleep problems (Wynchunk et al 2017) executive function and social cognitive deficits (Tatar and Cansiz, 2022), might effect their ability in establishing consistent bedtime routines and sleep habits for their children that then exacerbates their child's pre-sleep problem behaviours and sleep initiation problems (a possible reason why parents with both ADHD consistent features and insomnia probability had higher child sleep problem scores in our quantitative study (Chapter 4)). On the other hand, children's bedtime problems could impact parent's own routines and lead to sleep deficits (as found in our qualitative study (Chapter – 3)), which would then exacerbate ADHD like symptoms in the parents (Raman and Coogan, 2019). A third route iterates that although sleep problems and ADHD features between the adult and their offspring are highly heritable (Akingbuwa et al 2020; Takahashi et al 2020), a recent study also showed that children do not over or under inherit genetic liability for variable sleep features, such as insomnia, chronotype or sleep duration (Lewis et al 2021). This indicates that behavioural sleep problems related to initiation, maintenance and after waking behaviours might be attributed to the child's environment (which includes their family and household system) and their own developmental diversity (in cognition, behavioural or emotional regulation).

Our findings reiterated the possible impact of ADHD medication on the child's sleep (Chapter 3 and 4), which although has been previously mentioned (Coogan et al 2019). When underlining the impact of medication, the possible parental experiences to solve the problem also where highlighted (for example, consulting with physician to change timing/dosage, formulations, journey of reaching the optimal dose, or supplemental use of Melatonin).

Our thesis included the design of a parent questionnaire prototype (Childhood ADHD Sleep Scale) to assess sleep in their children diagnosed with ADHD (Chapter 5) which is the first such questionnaire that explores ADHD symptomatology specific sleep problems in children. Apart from the tool's good psychometric values for overall reliability, certain features of CASS, for example its domains being designed specifically based on the generated themes from our qualitative study, in addition to adhering to trends in the literature, added to its strength. A tool like CASS can be utilised both in research and the clinical setting, allowing exploration of sleep disturbances as experienced by children with ADHD, rather than present a multidimensional (sleep such as CSHQ) or concern (Daytime sleepiness) specific information.

The empirical studies in this thesis were based on data collected through subjective measures such as parental reports (on interviews and questionnaires) rather than a combination of objective tools (for example actigraphy) and subjective reports, thereby not controlling the confounding effect of reporter biases and differences in interpreting questionnaire items. This was a major limitation of this thesis. Use of both subjective and objective tools could highlight the factually measured macrostructural sleep properties, which could then be corroborated with the parent reports. Discrepancies between the two could be analysed and findings could be discussed taking into account the interaction of parent perceptions of sleep problems and the actual sleep problems seen in childhood ADHD.

In this thesis we did not use diagnostic measures of ADHD to ascertain the subtype and

severity of the condition, which can be considered as a limitation. Heightened prevalence of sleep disorder features were associated with increased ADHD symptom severity (Yin et al 2022). Moreover, ADHD inattentive presentation has previously been associated with higher daytime sleepiness (Mayes et al 2009), and children with ADHD combined, and hyperactivity/impulsivity presentations showed higher levels of overall sleep problems (Eyuboglu and Eyuboglu, 2017) as well as insomnia and nightmares (Grünwald and Schlarb, 2017) and periodic limb movements (Zambrano-sánchez et al 2013). However, the kind of sleep problems and their association with ADHD subtype is not consistently displayed in all studies; for example, Chiang et al (2010) reported the link between ADHD- combined and inattentive and daytime napping, and on the other hand, ADHD combined type is linked with circadian rhythm sleep problems, sleep talking and nightmares, and ADHD inattentive type with hypersomnia. The current literature therefore demonstrates overlap of sleep problems and symptom type, calling for more than an acknowledgement of the subtype, rather a detailed account of symptom presentation in the patient's environment.

The core ADHD clinical picture is associated with the presence of comorbid conditions (other neurodevelopmental disorders, learning disorders, and externalising and internalising disorders;Gnanavel et al 2019). These affect the nature and degree of challenges experienced by the child (Barkley, 1998; Shelton et al 1998). As our research question was to explore sleep in within the attention deficit and hyperactivity/impulsivity picture, we did not investigate this in terms of comorbidities, precisely to avoid overlap of symptoms which would prevent us from presenting an ADHD spectrum view of sleep problems. However, this itself became a limitation of this thesis. Emotional and behavioural comorbidities in ADHD have been associated with different sleep problems in childhood ADHD (Bondopadhyay, et al 2022). For example, daytime sleepiness is associated with more behavioural problems in the classroom (Lucas et al 2019), whereas sleep anxiety is related to greater internalizing comorbidities in these children (Mulraney et al 2016). Underlining the presence of comorbidities in our

investigations would have added to the clarity and richness of the information gathered. However, it is also important to note that ADHD is characterised by a somewhat dramatic bifurcation of its developmental course, especially during adolescence (Nigg et al 2020), where the clinical picture can become complicated by different psychopathologies. This indicates that during the preadolescent period which we have investigated, the child could be susceptible to a range of upcoming comorbidities, the majority of which might not be fully defined and rather in their dynamically fragile prodromal stage. In such a light, concentrating on sleep problems holistically based on the core ADHD symptoms provided our thesis more clarity.

In Chapter 4, information about comorbid psychopathology was not ascertained for parents, adding on as a weakness in the study. Psychiatric comorbidities have been found to have well established familial links and neurobiological commonalities with adult ADHD, with features of conditions such as mood, anxiety, substance use and personality disorders being commonly reported (Katzman et al 2017). This increases the challenge of reaching an accurate diagnosis and designing an effective management plan (Barkley and Brown, 2008). In ourstudy, we explored the presence of insomnia probability in parents. Comorbidities, including mood disorders, anxiety disorders, personality disorders and substance use disorder,are associated with higher prevalence of insomnia in adults with ADHD (Fadeuilhe et al 2021),thereby indicating such information's relevance for the current data's interpretation.

Children diagnosed with ADHD reported better quality of life for themselves as compared to their parent's reports (Sciberras et al 2011), underlining the discrepancy between the two reports. This makes it imperative to elicit both child and parent reports when investigating functional impairments related to ADHD. Our thesis did not directly collect information from children and depended on parent reports, which could be subject to over-generalisation of impairment in completing household tasks (including pre-sleep routines) and over-estimated sleep problems. A qualitative study exploring subjective experiences of parents

found that more than symptom alleviation, parents are concerned about overall functioning of their ADHD child and do not want long term dependence on medication (Wan et al 2016), which might explain why parents are more sensitive and vigilant to the day-to-day behaviours of the child that might seem to be affected by their condition (including sleep). The above point is further validated as chronic restriction of sleep (as seen in adults, Van Dongen et al 2003) when increased from 4-6 hours to 8 hours, the subjectively introspected level of sleepiness remained same (found otherwise by objective tests), thereby underlying that also the perceived level of cognitive impairment is undermined in case of self-reports. If such effects are apparent with adults, it could also be similar for parents who are only reporting their perception of the effects of sleep problems for their children. For this reason, gaining information from children and corroborating it with parent reports would have provided more reliable and critically analyzed results in this thesis.

Although the primary goal in this thesis was to underline the nature and impact of sleep problems in children diagnosed with ADHD, our thesis diverted to exploring the link between (screener measured) ADHD features and insomnia probability and sleep related attentional bias in a general adult population. Although this diversion could be considered a limitation of our thesis, this study explored an important psychological construct that is proposed to be a cognitive driver of insomnia, which itself is strongly over-represented in ADHD. Our findings indicated that sleep attentional biases did not appear to be a link between ADHD symptoms and poor sleep, but did underline that habitual alarm clock users demonstrate attention bias to sleep words, highlighting that social demands curtailing sleep could impact the person's cognitive processing of sleep related stimuli.

The majority of the investigations in this thesis were completed during the Covid-19 lockdown period and during the slow return to regular work and school schedules, which might have affected the nature of the results. During the lockdown related homeconfinement period,

59% children with ADHD reported decrease in their sleep duration, more bedtime delay, higher sleep anxiety and more difficulty falling asleep (Bruni et al 2021). Therefore, an unavoidable effect of the lockdown might have recorded higher levels of sleep problems in this population than what is usually experienced without the lockdown influence.

7.4 Future Directions

Our qualitative study (Chapter 3) analysed parent reports of their child's sleep problems and found that parents not only observe and report these difficulties but also share information on how this impacts them and the household, and the step they are taking to overcome these impacts. This indicates that parents are in a meaning-making process when managing their child's everyday functional demands (including those related to their sleep). The above trend resonates with the findings from Ringer et al (2019) who explained that this meaning making process is influenced by parental understanding of the child's ADHD diagnosis. This process includes facets such as experiencing difficulties, having an explanation and understanding the needs of their child, adjusting oneself, processing emotions and integration of ADHD with everyday life (Ringer, et al 2021). When it comes to sleep difficulties, future studies could delve deeper into how parents process these concerns and if there is a specific coping structure, which can be explored qualitatively (with parallel objective assessment of the child's sleep parameters). This would give a comprehensive understanding of the prevalence and impact of child's sleep problems in this population. Additionally, clinical trials to investigate the effect of a thorough sleep problem psychoeducation on parent's meaning making process could be helpful in designing clinician led awareness programs.

Although the field of ADHD research in the last number of decades has seen tremendous progress in characterizing the condition, the reason for individual differences in its impact, and the breadth of this impact, a significant gap remains between its associated clinical needs and the established interventions (Sonuga-Barke et al 2022). This is especially true for

sleep related difficulties. A number of behavioural and sleep hygiene related interventions have surfaced over the last decade (Malkani et al 2022; Sciberras et al 2022); however these are largely unpractised in the clinical settings. In the future, multisite clinical trials with an adequate sample size, should be initiated by country specific health boards, which could bring these interventions into the repertoire of the services provided for families in need.

Bidirectional links between sleep problems and ADHD in children highlight the importance of including sleep assessment as part of the initial psychological evaluation for the child when querying ADHD (Mulraney, et al 2016). Although the literature has mostly recommended initiating this assessment using generalised sleep assessment questionnaires (Hobson et al 2019), using an ADHD specific sleep problems assessing tool will be of particular clinical utility. This will allow the clinician to easily understand how the core ADHD and possible comorbid conditions are interfering with the child's sleep. With this goal in mind future research should design an ADHD specific sleep questionnaire or forward refinement of the CASS (Childhood ADHD sleep scale) prototype (Chapter 5).

Because of the marked heterogeneity in the nature of sleep problem manifestations in ADHD (comprising not only subtype-based differences, but also differences resulting from the interaction of comorbidities with core ADHD features, future research should include a thorough account of ADHD symptom nature, severity and comorbidities, which are explored not only through cross sectional design surveys, but longitudinal studies. Longitudinal studies would help decipher the course of the difficulties, underlining the possible precipitating, perpetuating and also the protective factors for the sleep problem. Heterogeneity in the ADHD clinical picture could also be attributed to gender differences, highlighting the neeed for future studies to recruit comparable number of males and female participants in the project.

Previous literature has focussed on finding cognitive functions and behavioural factors that are impacted by lack of sleep (Moreau et al 2013; Floros et al 2021); however, future

studies should explore the other direction of this relationship (ADHD-specific behavioural and cognitive features that impact the child's sleep). Our qualitative study emphasized on the plausible role of executive dysfunction in increasing sleep related behavioural problems in children with ADHD (Chapter 3). One promising avenue is exploring the role of executive function deficits in planning, focus, action, activating and monitoring in increasing bedtime routine inconsistency, difficulty completing pre-bed chores, transitioning to bedtime and winding down to sleep. This may not only demystify some attributional factors for these problems, but also adds to towards clinical utility, as behavioural techniques and psychoeducational guidance to parents can possibly be an effective tool to target these sleep problems. Future studies should also focus on delineating the role of sensory processing difficulties in influencing sleep initiation and maintenance for children with ADHD. Clinical trials using items such the Ball blanket have shown promise (Larsson, et al 2021), while non-intervention studies have consistently linked sleep problems with sensory sensitivities in this population (Ghanizadeh, 2011; Hartman, et al 2022). Well-designed RCTs trialling sensory based sleep interventions would be an important addition to the existing repertoire of multifaceted interventions.

7.5 Conclusion

In this thesis we underlined the nature of sleep in childhood ADHD, then proceeded to explore parental reports of their child's sleep qualitatively and quantitatively, and finally presented the prototype for a parent rated sleep questionnaire while acknowledging the importance of a condition specific sleep assessment tool in this field. We also explored the role of attentional biases in sleep problems among older cohorts. While capturing the varied macrostructural and microstructural alterations of sleep in this population, we underlined its consequences both on the young person with ADHD and their families. Bidirectional interactions between sleep and core ADHD features further established the justification for

moving beyond the use of generalized sleep questionnaires in this population, which led us to create the prototype for CASS (Childhood ADHD Sleep Scale, a parent report sleep scale assessing ADHD specific sleep problems in children). Based on our learning we can conclude that ADHD, characterized as the presence of distinct cognitive, motor and behavioural abilities results from maturational dysregulation of the frontal and prefrontal cortical structures and connections, which deems ADHD not a disorder, or dysfunction, but a state of functioning. This state of functioning is not consistent with the psychosocial and psychomotor expectations related to the chronological age of the person (Leisman and Melillo, 2022) which also manifests in their sleep and wake behaviours. Both being regulated by the central nervous system, sleep and ADHD have a strong neurobiological overlap (Miano, 2012), with consistent evidence of bidirectionality between the two (Scott et al 2013). Presence of sleep disturbance in childhood ADHD has been well documented (Bondopadhyay et al 2022), although sometimes exaggerated with subjective reports (Cortese et al 2009). ADHD cannot be perceived as a daytime disorder, and as result future research using adaptive methodologies are needed to create optimally personalized treatment protocols addressing sleep disturbances in this population. Specialists working with children with ADHD will require skills and training to effectively manage sleep problems in this population. Let us not sleep over this!

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Appendices

APPENDIX A:

Childhood ADHD Sleep Scale (CASS)

CHILDHOOD ADHD SLEEP SCALE (CASS)

Name of child…… Age…… Gender…….

Name of parent……. Relationship with child…….

Instructions: This scale includes questions which will help us understand the nature of your child's sleep. Please select the option that best describes your child's behaviors.

Item	(5) Strongly agree	(4) Somewhat agree	(3) Neither agree nor disagree	(2) Somewhat disagree	(1) Strongly disagree
Child is very active, talkative, or busy making plans at bedtime.					
Child needs consistent routines in the hour before bedtime (e.g. snack, bath, reading)					
Childs can only fall asleep in their carer's bed/not their own bed					
Child resists going to bed					
Child struggles to sleep alone, is scared of the dark or needs caregiver in the bedroom to fall asleep.					
Child needs special blankets or other bedclothes to fall sleep.					
Child is very sensitive to their bedroom's temperature, brightness, or noise.					
Child typically takes longer than 30 minutes to fall asleep.					
Child often reports being anxious or worried when trying to fall asleep.					
Child is often upset about not being able to sleep					
Child often awakens during the night					
Child struggles to fall back asleep if they wake at night					
Child calls on caregiver to seek reassurance during the night or tries to get into their carers' bed					
Child often wakes very early in the morning regardless of when they fell asleep the night before					

Item	(5) Strongly agree	(4) Somewhat agree	(3) Neither agree nor disagree	(2) Somewhat disagree	(1) Strongly disagree
Child is often still sleepy for the first hour after wakening					
Child has significantly worse sleep than other children that I am familiar with					
Child's sleep is more difficult on school days than on days during the weekend or school holidays					
On a schoolday morning, the child need an alarm clock or to be woken by someone else.					
Child often wets the bed at night.					
Child often talks during sleep.					
Child often moves his hands and legs during sleep.					
Child usually snores, snorts, or gasps during sleep.					
Child often sleepwalks.					
Child often has nightmares.					
Child often grinds his teeth during sleep.					
Child often awakes screaming and sweating (night terrors)					
Child usually performs their morning routine at a slow pace and seems tired.					
Child easily loses their temper during morning routine.					
Child is often sleepy during the day.					
Child often needs a nap, or falls asleep, during the day.					
Child is markedly more emotional, difficult, or inattentive after a bad night's sleep					

Item	(5) Strongly agree	(4) Somewhat agree	(3) Neither agree nor disagree	(2) Somewhat disagree	(1) Strongly disagree
My own sleep is negatively impacted by my child's sleep problems.					
The sleep of other household members is negatively impacted by my child's sleep problems.					
Child's sleep problems negatively impact on my relationships with significant other adults.					
I am very concerned about my child's sleep.					

Please answer the following questions about your child's sleep timing:

1. What time does your child go to bed on weekends/holidays…….

2. What time does your child wake on weekends/holidays……

3. What time does your child go to bed on school days/weekdays……

4. What time does your child wake on school days/weekdays……...

If your child is currently using prescribed anti-ADHD medication or Melatonin for sleep, please answer the following questions about your child:

1. My child's ADHD medication makes it difficult to fall asleep……

2. My child's ADHD medication makes it difficult for them to sleep through the night without waking…….

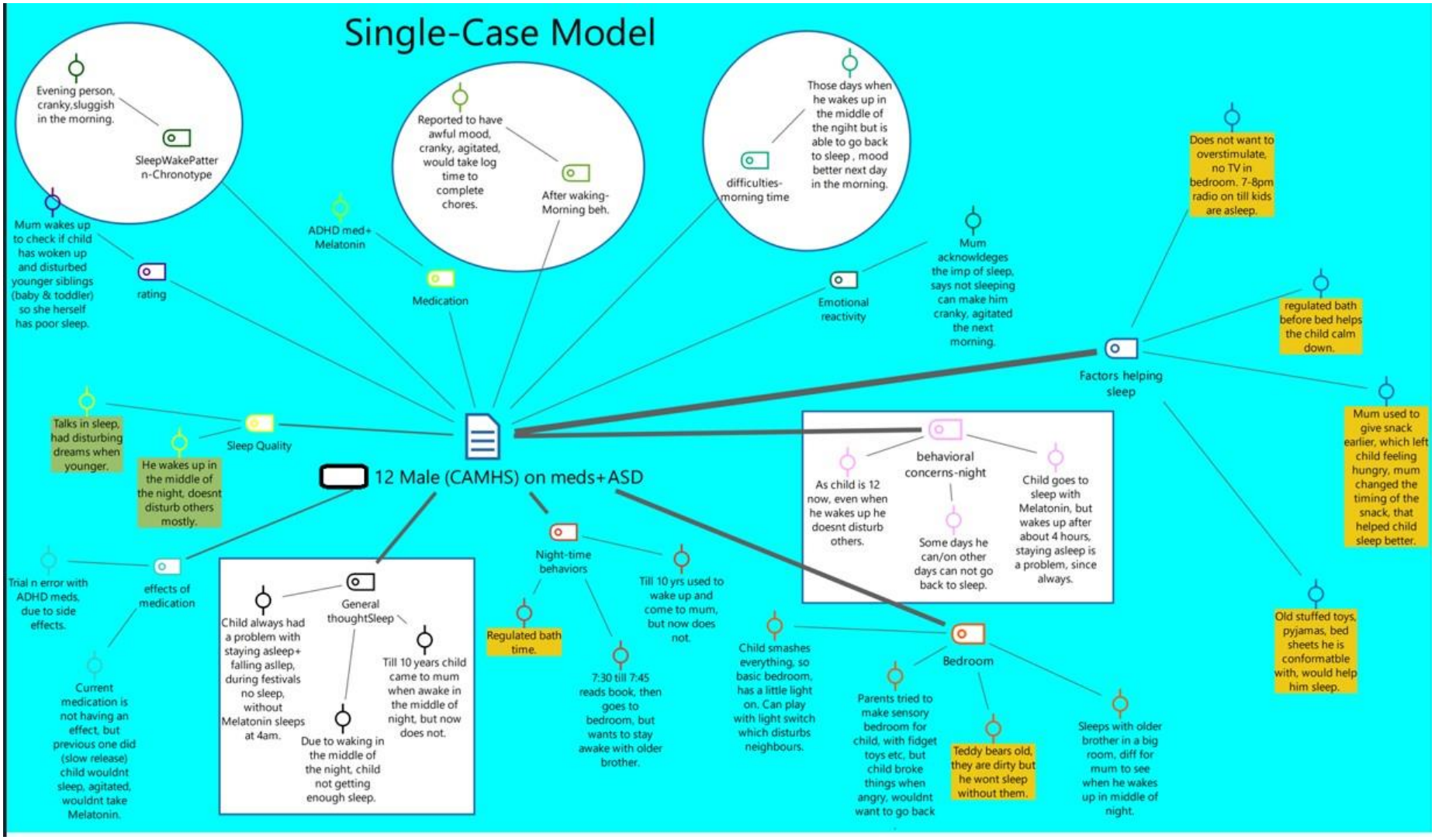
3. My child's ADHD medication makes it difficult for them to wake up in the morning……

4. If medication for sleep is taken by the child (e.g. melatonin), it helps them fall asleep at night…….

5. If medication for sleep is taken by the child (e.g. melatonin), it helps them sleep through the night……

APPENDIX B:

Example of one interview visual map


Single-Case Model
Evening person, cranky,sluggish in the morning.
SleepWakePatter n-Chronotype
Mum wakes up to check if child has woken up and disturbed younger siblings (baby & toddler) so she herself has poor sleep.
rating
Reported to have awful mood, cranky, agitated, would take log time to complete chores.
After waking-Morning beh.
ADHD med+ Melatonin
Medication
Those days when he wakes up in the middle of the ngiht but is able to go back to sleep , mood better next day in the morning.
difficulties-morning time
Emotional reactivity
Mum acknowldeges the imp of sleep, says not sleeping can make him cranky, agitated the next morning.
Does not want to overstimulate, no TV in bedroom. 7-8pm radio on till kids are asleep.
regulated bath before bed helps the child calm down.
Factors helping sleep
Mum used to give snack earlier, which left child feeling hungry, mum changed the timing of the snack, that helped child sleep better.
Old stuffed toys, pyjamas, bed sheets he is conformatble with, would help him sleep.
Talks in sleep, had disturbing dreams when younger.
He wakes up in the middle of the night, doesnt disturb others mostly.
Sleep Quality
12 Male (CAMHS) on meds+ASD
behavioral concerns-night
As child is 12 now, even when he wakes up he doesnt disturb others.
Some days he can/on other days can not go back to sleep.
Child goes to sleep with Melatonin, but wakes up after about 4 hours, staying asleep is a problem, since always.
Trial n error with ADHD meds, due to side effects.
effects of medication
Current medication is not having an effect, but previous one did (slow release) child wouldnt sleep, agitated, wouldnt take Melatonin.
General thoughtSleep
Child always had a problem with staying asleep+ falling asllep, during festivals no sleep, without Melatonin sleeps at 4am.
Due to waking in the middle of the night, child not getting enough sleep.
Till 10 years child came to mum when awake in the middle of night, but now does not.
Night-time behaviors
Regulated bath time.
7:30 till 7:45 reads book, then goes to bedroom, but wants to stay awake with older brother.
Till 10 yrs used to wake up and come to mum, but now does not.
Child smashes everything, so basic bedroom, has a little light on. Can play with light switch which disturbs neighbours.
Bedroom
Parents tried to make sensory bedroom for child, with fidget toys etc, but child broke things when angry, wouldnt want to go back
Teddy bears old, they are dirty but he wont sleep without them.
Sleeps with older brother in a big room, diff for mum to see when he wakes up in middle of night.