IMPACT OF SLEEP ON DAYTIME FUNCTIONING AND RESPONSE TO
TREATMENT IN CHILDREN WITH ADHD

by

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Abstract

Sleep is critical for healthy development; however many children experience sleep problems. Both typically developing (TD) children and those with attention-deficit/hyperactivity disorder (ADHD) commonly report prolonged sleep onset latency (SOL) and short sleep duration. The primary objective of this dissertation was to better understand the relationship between sleep and ADHD in school-aged children. This dissertation consists of a narrative review of the sleep restriction literature in school-aged children, and two empirical studies. Results from the narrative review found that all of the eight experimental sleep restriction studies examined sleep restriction/deprivation compared to extended/optimized or baseline sleep. As such, the impact of sleep restriction in school-aged children is unknown. The first empirical study was a within- and between-subjects experimental sleep restriction study. Participants were children with ADHD (n = 18), and age- and sex-matched TD children (n = 18). Participants experienced a Restricted condition (i.e., time in bed (TIB) reduced by 1 h per night for six nights), and a Typical condition (i.e., TIB based on habitual sleep). Results of actigraphy data showed that children had significantly less TIB and total sleep time (TST). However, SOL and wake after sleep onset (WASO) were shortened during Restricted condition, thereby reducing the effect of the restriction. There was a significant effect of sleep condition on objectively measured attention and subjectively measured emotion. Children with ADHD were not differentially affected by sleep restriction compared to TD children. In the second empirical study, baseline sleep data were explored as predictors of treatment effectiveness and side-effects for children with ADHD (N = 50) undergoing a stimulant medication trial. Results showed that pre-treatment parent-rated sleep duration predicted treatment effectiveness (i.e., ADHD symptom reduction), and subjective baseline sleep problems predicted more insomnia side-effects during medication, but not global side-effects. Actigraphy did not significantly predict treatment effectiveness or side-effects of any kind. Results of these studies provide evidence for the importance of assessing and monitoring sleep in both TD children and those with ADHD. These results also highlight that sleep plays an important role in healthy functioning, and may be helpful in predicting treatment response for children with ADHD.

List of Abbreviations Used

ADHD = attention-deficit hyperactivity disorder

ART = affective response task

CBCL = Child Behavior Checklist

CEMS = Children's Emotion Management Scales

CCTT = Children's Color Trails Test

CPRS = Conners' Parent Rating Scale

CTRS = Conners' Teacher Rating Scale

CPSS = Child's Pictorial Sleepiness Scale

CPT = Continuous Performance Test

CSHQ = Children's Sleep Habits Questionnaire

CSSR = Child Sleep Self Report

ECG = electrocardiogram

EEG = electroencephalogram

EMG = electromyogram

EOG = electrooculogram,

ERC = Emotion Regulation Checklist

FBRC = faded bedtime with response cost

FSIQ = full scale intelligence quotient

h = hour (s)

IAPS = International Affective Picture System

MESS = Modified Epworth Sleepiness Scale

Min = minutes

MSLT = multiple sleep latency test

N; n = sample size

PFC = prefrontal cortex

PSG = polysomnography

RA = research assistant

RAR = research assistant report

Res = restricted

RM = repeated measures

RT = reaction time

SD = standard deviation

SE = sleep efficiency

SEQ = Sleep Evaluation Questionnaire

SOL = sleep onset latency

STM = short-term memory

TD = typically developing

TIB = time in bed

TST = total sleep time

Typ = typical

WASO = wake after sleep onset

WM = working memory

Acknowledgements

Chapter 1: Introduction

ADHD and Sleep

Attention-deficit/hyperactivity disorder (ADHD) is the most common childhood

neurodevelopmental disorder with a prevalence of approximately 5-7% (Wilcutt, 2012).

The core symptoms of ADHD are difficulties with attention, hyperactivity, and

impulsivity (American Psychiatric Association, 2013). ADHD is also associated with

other daytime difficulties including deficits in working memory (Martinussen, Hayden,

Hogg-Johnson, & Tannock, 2005), and emotional problems such as emotional

dysregulation and emotional lability/negativity (Graziano & Garcia, 2016). In addition to

daytime impairments, it is well documented that there is a relationship between ADHD

and sleep problems. Prevalence estimates range from 25-50% of children with ADHD

reporting sleep disturbances, particularly prolonged sleep onset latency (SOL) and

shortened sleep duration (Owens, 2005; Spruyt & Gozal, 2011; Yoon, Jain, & Shapiro,

2012). These sleep problems have been associated with daytime sleepiness (Lecendreux,

Konofal, Bouvard, Falissard, & Mouren-Siméoni, 2000), as well as a range of problems

including academic problems (Langberg, Dvorsky, Marshall, & Evans, 2013), and

executive functioning difficulties (Moreau, Rouleau, & Morin, 2013). Sleep problems in

children with ADHD have also been significantly associated with children missing more

school, poorer parental mental health, and family functioning stress for the family as a

whole (Sung, Hiscock, Sciberras, & Efron, 2008).

Primary sleep disorders such as obstructive sleep apnea, restless legs syndrome,

and periodic limb movements have been associated with ADHD. These disorders are

sometimes misdiagnosed as ADHD (Brown & McMullen, 2001) because they can cause

secondary problems that resemble symptoms characteristic of ADHD (Hvolby, 2015; Spruyt & Gozal, 2011; Yoon et al., 2012). However, the most common sleep disturbance reported for children with ADHD is insomnia, defined as repeated difficulties with initiating sleep, shorter sleep duration, less sleep consolidation, or sleep quality despite adequate opportunities for sleep, resulting in daytime impairments (International Classification of Sleep Disorders-Third Edition [ICSD-3]; American Academy of Sleep Medicine, 2014). Specifically, sleep onset insomnia, characterized by long SOL and reduced overall sleep duration has been reported as the most common sleep problem for children with ADHD regardless of medication status (Brown & McMullen, 2001; Corkum, Moldofsky, Hogg-Johnson, Humphries, & Tannock, 1999; Ganelin-Cohen & Ashkenasi, 2013; Hvolby, 2015; Spruyt & Gozal, 2011; Van der Heijden, Smits, Van Someren, Ridderinkoff, & Gunning, 2007).

The most common treatment of ADHD is stimulant medication, further complicating the relationship between ADHD and sleep problems. Approximately 60-70% of children with ADHD are treated with stimulant medication (Brault & Lacourse, 2012; Konofal, Lecendreux, & Cortese, 2010; Stein, Weiss, & Hlavaty, 2012; Visser et al., 2014) despite the known side-effects of reduced sleep duration and increased SOL (Hvolby, 2015; Ironside, Davidson, & Corkum, 2010; Lee et al., 2011; Stein et al., 2012; Wilens et al., 2005). There is some evidence that children with pre-existing sleep problems have more sleep problems while on medication than children without pre-existing sleep problems (Becker, Froehlich, & Epstein, 2016), indicating that identifying pre-treatment sleep problems may be particularly important in determining possible insomnia side-effects. In summary, symptoms of ADHD may be exacerbated by sleep

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problems, sleep problems may mimic symptoms of ADHD, and treatment of ADHD symptoms with stimulant medication may cause or worsen sleep problems (Hvolby, 2015; Stein et al., 2012).

Theoretical Perspectives on the Relationship Between ADHD and Sleep

The relationship between ADHD and sleep problems in children is often described as complex and multifaceted, and is generally not well understood (Hvolby, 2015; Spruyt & Gozal, 2011; Yoon et al., 2012). There are three common theoretical frameworks for understanding the relationship between ADHD and sleep problems: the circadian delay hypothesis, the nocturnal activity hypothesis, and the hypoarousal hypothesis.

The circadian delay hypothesis. There is some research to suggest that medication-free children with ADHD have prolonged sleep onset due to a delayed evening melatonin release (Van der Heijden, Smits, Van Someren, & Gunning, 2005). In the adult literature, studies have shown that ADHD symptom severity is significantly associated with delayed sleep onset and daytime sleepiness. Additional support for this hypothesis from the pediatric literature is that children with ADHD have stronger circadian evening tendencies compared to TD children (Gruber et al., 2012). Furthermore, intervention studies have shown treatment with melatonin resulted in improved sleep: shorter SOL and longer sleep duration based on actigraphy, and reduced SOL problems based on parent report (Van der Heijden et al., 2007). However, no improvements in daytime ADHD symptoms were observed (Van der Heijden et al., 2007).

The nocturnal activity hypothesis. Several researchers have posited that ADHD is a 24 h disorder with increased motor activity during sleep as well as during the daytime hours, resulting in increased nocturnal sleep disturbance (Corkum & Coulombe, 2013; Hvolby, 2015; Konofal et al., 2010). Studies supporting this hypothesis have examined nocturnal motor activity in children using infrared camera technology and found that children with ADHD moved more during sleep, and movements were longer than in TD children (Konofal, Lecendreux, Bouvard, & Mouren-Siméoni, 2001). While treatment of ADHD symptoms with methylphenidate (MPH) in children has resulted in prolonged SOL and reduced sleep duration (Hvolby, 2015; Ironside et al., 2010; Lee et al., 2011; Stein et al., 2012; Wilens et al., 2005), there is some evidence in the adult literature that treatment with MPH reduces nocturnal motor activity and improves sleep quality (Kooij, Middelkoop, van Gils, & Buitelaar, 2001). Pediatric researchers also found that children spent more time in light sleep, and the number of night awakenings were reduced while taking stimulant medication (Kim et al., 2010). These findings provide evidence for a possible relationship between high levels of motor activity during sleep and the sleep disturbances commonly reported in children with ADHD.

The hypoarousal hypothesis. Many symptoms of ADHD are also symptoms of insomnia. Research suggests that common neurobiological processes may be involved in the symptom presentation of both disorders (Yoon et al., 2012). Specifically, the pre-frontal cortex plays a role in the regulation of arousal, and in the regulation of attention and affect (Brown & McMullen, 2001). Therefore, the hypoarousal hypothesis of ADHD and sleep problems is based on the concept that symptoms of inattention or lowered vigilance are in fact symptoms of lowered arousal/alertness and that excessive motor

activity or restlessness is a strategy used to help maintain arousal (Brown & McMullen, 2001). Evidence for this hypothesis comes from studies examining daytime sleepiness as an indicator of arousal where children with ADHD are sleepier than their TD peers based on objective measures of sleep (Golan, Shahar, Ravid, & Pillar, 2004; Lecendreux et al., 2000; Cortese, Konofal, Yateman, Mouren, & Lecendreux, 2006). Data from the adult literature also suggests that there are associations between inattention and alertness/daytime sleepiness (Kallepalli et al., 1997).

Research Questions in the Literature

Children with ADHD experience significant daytime impairments of attention, emotion, and cognitive functioning, and also commonly report night-time impairments, including prolonged SOL and reduced overall sleep duration. Researchers have highlighted the need for more experimental research to better understand the causal relationship between ADHD and sleep, to both inform assessment considerations, and develop multimodal approaches of interventions for day and night symptoms of ADHD (Spruyt & Gozal, 2011). Three broad questions about the relationship between ADHD and sleep are summarized below along with the aims of this dissertation in addressing these questions.

Research question 1: What is the state of the literature on the impact of sleep in school-aged children for both typically developing and children with ADHD and what are the gaps in this body of research? Chapter 2 of this dissertation is a narrative review focused on reviewing and synthesizing the existing research literature on experimental sleep manipulation studies in school-aged children and the impact on daytime functioning. Given the relationship between ADHD and sleep problems, the

review also included sleep restriction in children with ADHD. Information on the sleep restriction methods, outcome measures of daytime functioning, as well as inconsistencies and gaps in the literature were of particular interest to inform design of the empirical studies that make up Chapters 3 and 4 of this dissertation. This review was paramount as no reviews to date have specifically focused on sleep restriction in school-aged children and the impact on daytime functioning. Furthermore, the results of the narrative review were used to determine the best methods and study design for experimental sleep restriction in school-aged children, both TD and children with ADHD.

Research question 2: What is the impact of mild cumulative sleep restriction on both subjectively rated and objectively measured sleep and daytime outcomes, in children with ADHD compared to healthy, TD controls? Based on results of the narrative review (Chapter 2), the first empirical study in this dissertation (Chapter 3) was designed to examine daytime functioning (i.e., attention, emotions, cognitive functioning) following experimental sleep restriction compared to controlled typical sleep. Previous experimental studies compared sleep restriction to either sleep extension, sleep optimization, or baseline sleep. No previous experimental study has compared the effects of sleep restriction to those of controlled typical sleep (which was based on the habitual sleep schedule) on daytime functioning. Therefore, previous study results did not determine whether change in daytime functioning was due to improvement as a result of sleep extension/optimization or deterioration due to sleep restriction. Furthermore, despite the relationship between sleep and negative daytime outcomes in children with ADHD, only one previous experimental sleep restriction study included a sample of children with ADHD. As such, there is very little data available on the impact of sleep

restriction in children with ADHD. Finally, it has been noted in the literature that both stimulant medication and co-morbid mental health symptoms are confounding factors in the relationship between sleep and ADHD, and that more research in children who are medication naïve, and children with ADHD with no co-morbid mental health symptoms, is needed to better understand this relationship (Corkum & Coulombe, 2013; Hvolby, 2015; Konofal et al., 2010).

Previous findings suggest that mild cumulative sleep restriction (i.e., 1 h sleep restriction nightly), a common experience for many children, may be more impairing than acute sleep deprivation. Additionally, sleep restriction at bedtime (i.e., delayed bedtime by 1 h), parallels the primary problem in children with ADHD (i.e., prolonged SOL and subsequent shortened sleep duration), the main impact of stimulant medication, and one of the primary sleep problems in TD children as well (i.e., insomnia). Therefore, examining the impact of experimentally delayed bedtime and shortened sleep duration in children with ADHD may help clarify the impact of shortened sleep on daytime functioning in both children with and without ADHD, as well as the effects of medication.

Research question 3: Is there a relationship between pre-treatment sleep and treatment response to stimulant medication (effectiveness and negative sleep side-effects) for children with ADHD on stimulant medication? There is a significant relationship between ADHD and sleep problems; in particular prolonged SOL and shortened sleep duration are the most common symptoms in children with ADHD (even before treatment). These sleep problems are also the main sleep side-effect of stimulant medication. In particular, the relationship between pre-treatment sleep problems taken

together with both the therapeutic effect of medication, and the negative sleep side-effects (i.e., insomnia) were of interest. Previous studies have examined response to stimulant medication in children with ADHD in the absence of a placebo condition (Kim et al., 2010), in children with previous medication experiences (Wilens et al., 2005), or using only a single item on a questionnaire to determine baseline sleep problems (Becker et al., 2016). Therefore, the second empirical study (Chapter 4) of this dissertation was designed to help determine how medication-naïve children with ADHD respond to a course of stimulant medication compared to a placebo condition, using pre-treatment sleep information from a well-validated sleep questionnaire. This study was important as the results may help identify children who are more or less likely to experience negative sleep side-effects. Then, pre-treatment interventions could be put into place, including parent education and promotion of healthy sleep habits. With healthy sleep habits in place, children and families would be better prepared to manage potential negative sleep side-effects, thus increasing medication adherence and ultimately the therapeutic benefits of medication.

Overview of Dissertation Objectives

The main objective of this dissertation was to further the understanding of the relationship between ADHD and sleep in a sample of medication naïve, rigorously diagnosed children, with no comorbid mental health disorders, aged 6-12 years. The specific goals of this dissertation were to: 1) review and synthesize the literature on sleep restriction in school-aged children, both TD and children with ADHD, 2) restrict sleep in school-aged children and examine the impacts on both subjective and objective measures of attention, emotion, and cognitive functioning using experimental methods to examine

causality, and 3) determine whether subjectively rated baseline sleep duration and SOL could be used to predict therapeutic effect and side-effects of stimulant medication. These goals were achieved through three manuscripts. The first manuscript (Chapter 2) is a broad narrative review of the literature on sleep restriction and the impact on daytime functioning in children. The second manuscript (Chapter 3) describes an experimental sleep restriction study of children with ADHD and age- and sex-matched TD peers. The impact of sleep restriction on daytime functioning was examined between and within-groups using repeated-measures multivariate analysis of variance (RM-MANOVA). The third manuscript (Chapter 4), describes an empirical study that used hierarchical regression analyses to examine the ability of baseline sleep to predict therapeutic effect and side-effects of stimulant medication in children with ADHD. The final chapter of this dissertation (Chapter 5) is a general discussion of findings, with commentary on how the research conducted for this dissertation furthers the knowledge about the relationship between ADHD and sleep, and closes with future directions for research and the clinical implications of this research.

Chapter 2: The Impact of Sleep Restriction on Daytime Functioning in School-Aged Children with and without ADHD: A Narrative Review of the Literature

The manuscript based on this narrative review is presented below. Readers are advised that Fiona Davidson, under the supervision of Dr. Penny Corkum, was responsible for the research question, the review methodology, critical analysis of the included papers, and all aspects of the writing process. She received critical editorial feedback from her dissertation committee members (Dr. Benjamin Rusak and Dr. Christine Chambers).

Abstract

The purpose of this narrative review was to synthesize the existing literature on the impact of sleep on daytime functioning in both typically developing (TD) children and children with attention-deficit/hyperactivity disorder (ADHD). Correlational studies in children suggest that insufficient sleep and impaired daytime functioning are significantly associated, however this does not address the causal relationships between sleep and daytime functioning. The review results indicated that there is limited experimental sleep manipulation research in children. In the eight studies that employed experimental methods to examine sleep restriction, the consequences of insufficient sleep were greatest for attention, and inconsistent for other domains such as cognition and emotion regulation. Despite the significant co-occurrence of ADHD and sleep problems, the experimental sleep research focused on the daytime impact of shorter sleep in children with ADHD is extremely limited and as such more research is needed.

Introduction

All humans sleep; there is a large body of research that has demonstrated that sleep is critically important for daytime functioning such as cognition (Goel, Rao, Durmer, & Dinges, 2009). Historically, sleep was considered to be a general restorative process where the brain and the body were mostly inactive. This concept was revised when rapid-eye movement (REM) sleep, a state of sleep characterized by rapid eye movements, decreased muscle tone, and desynchronized, highly active cortical electroencephalogram (EEG), was discovered in the early 1950s (Dement, 2005). The large body of sleep research that exists indicates that there is no single function of sleep; rather, sleep plays a role in many functions such as attention, emotion regulation, and cognition (e.g., learning and memory), as well as for supporting healthy cardiovascular, metabolic, and immune systems (Buysse, 2005; Poulin, Jung Kim, & Germain, 2011). Given these functions, it is not surprising that recent studies in both humans and animals have shown that poor sleep (i.e., poor sleep quality and quantity) has adverse effects on alertness, mood, learning, emotional processing, and cognitive functioning (Buckhalt, 2011; Buysse, 2005). Consequently, many sleep researchers are interested in understanding the role of insufficient sleep on both psychological and physical health.

The goal of this narrative review is to synthesize the literature on the psychological impact of insufficient sleep in children aged 6-12 years with a particular focus on the impact of insufficient sleep in children with ADHD. The International Classification of Sleep Disorders (ICSD-3; American Academy of Sleep Medicine, 2014) identifies seven major categories of sleep disorders, with insomnia and its component symptoms being the most common in children and adults. Insomnia is defined by the

ICSD-3 as repeated difficulty with initiating sleep, sleep duration and consolidation, or sleep quality that occurs despite adequate opportunities for sleep, and results in daytime impairment. Sleep restriction studies are often used as a way to better understand the impact of insomnia. As such, this paper is focused on sleep restriction and its impact on daytime functioning in school-aged children with and without ADHD. First, an overview of the methods used to measure sleep, and the operational definitions used in the literature are reviewed. Then, to provide context for the state of the literature in pediatric sleep, the adult literature is briefly summarized. Next, an overview of the impact of sleep restriction in children, both correlational studies and experimental studies is provided. The relationship between sleep and mental health, in particular ADHD, is then discussed, followed by a review of the existing data on the impact of sleep restriction in children with ADHD. Finally, the impact of stimulant medications on sleep in children with ADHD are briefly reviewed.

Measuring Sleep and the Language Around Sleep Loss

There are two broad ways of measuring sleep: 1) sleep can be measured subjectively using measures such as sleep diaries or questionnaires, and 2) sleep can be measured objectively using measures such as polysomnography (PSG) or actigraphy. PSG involves the measurement of a number of physiological and behavioural variables including EEG, electrocardiogram (ECG), electrooculogram (EOG), electromyogram (EMG), respiratory effort, airflow, and continuous oxygen saturation recording during an overnight sleep assessment. Actigraphy is used to estimate sleep parameters by measuring motor activity using an accelerometer-based device. Actigraphs resemble a small wristwatch and are worn on the non-dominant wrist. Previous studies have shown

that actigraph data provide valid and reliable estimates of when participants are asleep and awake, as well as a means of assessing sleep quality variables such as sleep latency and duration (Acebo et al., 1999; de Souza et al., 2003; Sadeh et al., 1995; Tryon, 2004). Actigraphy has been found to have good face validity and reliability, which has been documented in numerous studies. Studies have found a high rate of agreement (85-90%) between actigraphy and PSG, and actigraphs have been found to distinguish between sleep disturbed and control children (Ancoli-Israel, et al., 2003; Sadeh & Acebo, 2002).

In the sleep literature, there are different terms used to describe sleep loss, including sleep deprivation and sleep restriction. These terms are often used interchangeably. While there are no formal definitions, sleep deprivation is often used to describe total or partial sleep loss during which individuals are asked to refrain from sleeping for an entire night, or the majority of a night (e.g., only spend 2 h sleeping). Sleep restriction often refers to the imposition of a later sleep onset and/or earlier wake time than is typical, resulting in a less extreme degree of sleep loss. For example, a mild sleep restriction may be defined as bedtime delayed by an hour. Acute sleep restriction/deprivation refers to sleep loss over the course of one or two nights rather than several nights. Cumulative or chronic sleep restriction/deprivation refers to getting less sleep than is physiologically recommended to maintain optimal functioning over a number of nights (Reynolds & Banks, 2010).

The relationship between sleep variables (e.g., sleep duration) and daytime functioning variables (e.g., performance on cognitive tasks) can be examined by way of correlational methods. Correlational research is valuable in determining where possible relationships may exist among sleep and daytime functioning variables; however, causal

relationships cannot be determined. Experimental sleep manipulation studies control sleep variables by randomly assigning participants to spend a certain amount of time in bed (TIB), to produce either acute sleep deprivation or a cumulative sleep restriction. Sleep can also be extended, where TIB is more than what is typical, or optimized, which is when TIB is controlled to allow for full sleep satiation and to minimize the effect of any previously accrued sleep debt. For children, previous studies have used either 10 h TIB (Biggs et al., 2010; Fallone, Acebo, Arnedt, Seifer, & Carskadon, 2001; Fallone, Acebo, Seifer, & Carskadon, 2005; Peters et al., 2009) or 11 h TIB (Randazzo, Muehlbach, Schweitzer, Walsh, 1998) for sleep optimization. Performance following experimentally restricted sleep is then compared to performance following either extended, optimized, or baseline sleep (i.e., habitual sleep). By controlling the sleep variables of interest, causal relationships can be inferred between sleep and daytime functioning outcome variables.

Effect of Sleep Restriction in Adults

The impact of insufficient sleep in adults has received considerable research attention, and findings suggest that sleep loss can have negative impacts across multiple functions. Two recent systematic reviews of adult data including 70 studies ($N = 1,533$; Lim & Dinges, 2010) and 24 studies ($N = 1,197$; Fortier-Brochu et al., 2012) indicated that shortened sleep duration has an impact on several cognitive functioning domains, including working memory, short term, and episodic memory (Fortier-Brochu et al., 2012; Lim & Dinges, 2010), problem solving (Fortier-Brochu et al., 2012), simple attention, and complex attention (Lim & Dinges, 2010).

Research also showed that cumulative sleep restriction of 6 h TIB per night for 14 nights was as detrimental to behavioural alertness as one night of complete sleep deprivation (Van Dongen, Maislin, Mullington, & Dinges, 2003). Furthermore, participants who spent 4 h TIB for 14 nights reached the same level of impairment as those who underwent three nights of complete sleep deprivation (Van Dongen et al., 2003).

It is well established that insomnia is a common symptom experienced by adults with mental health disorders such as depression, anxiety, and ADHD. For example, one of the diagnostic criteria for depression is the presence of insomnia or hypersomnia most days, and one of the criteria for anxiety is sleep disturbance such as difficulty falling asleep, staying asleep, or restless unsatisfying sleep (American Psychiatric Association, 2013). Research findings also support the relationship between sleep problems and symptoms of anxiety and depression (Furihata et al., 2015; Leblanc, Desjardins, & Desgagne, 2015). Not only are sleep problems integral to mental health symptoms, there is evidence that sleep disruption may contribute to generating symptoms associated with mental health disorders. Interestingly, a study of healthy adults revealed that based on subjective measures collected prior to and after sleep deprivation, there were increased scores on clinical scales of psychopathology including: somatic complaints, anxiety, depression, and paranoia (Kahn-Greene, Killgore, Kamimory, Balkin, & Killgore, 2007). The scores were not elevated to values that met the threshold for clinical diagnosis; however, given that otherwise healthy individuals showed significant increases in symptoms of psychopathology following sleep deprivation, individuals with pre-existing mental health conditions are likely to have an even more profound response to sleep loss.

Furthermore, results from recent studies have shown that adults who participated in cognitive behavioural therapy (CBT) for insomnia had both improved sleep and improved depression scores over controls (Wagley, Rybarczyk, Nay, Danish, & Lund, 2013). Results also demonstrated the combination of brief behavioural therapy for insomnia and treatment as usual for depression yielded reduced insomnia and depression ratings (Watanabe et al., 2011). These findings collectively suggest that the relationship between sleep problems and mental health problems are likely bidirectional in nature.

The amount and scope of sleep literature in adults is much broader than the pediatric literature with respect to the daytime impacts of insufficient sleep. The subsequent sections of this paper will highlight what is known about insufficient sleep in children and where some of the gaps in the literature still exist.

Effect of Sleep Restriction in Children

The literature to date on sleep restriction in otherwise healthy, TD children and the resulting daytime impact is mostly based on correlational studies, while experimental studies are limited. Compared to research on TD children, there is substantially less research on children with mental health problems and the vast majority of this research is correlational.

There are currently no empirically based recommendations for sleep duration for children. The National Sleep Foundation (NSF) recently released recommendations suggesting that school-aged children (aged 6-12) should get approximately 10 h of sleep over a 24 h period (Hirshkowitz et al., 2015), while the Canadian Society for Exercise Physiology (CSEP) recently released 24 h movement guidelines for children which includes 9 to 11 h of sleep per night (CSEP, 2016). There is some controversy around

sleep duration recommendations in the pediatric sleep research field, given the lack of

empirical evidence for them (Matricciani et al., 2012). It is often stated that sleep

duration has decreased over time, and while there is controversy associated with this

statement, there is general agreement and concern for insufficient sleep and the

subsequent daytime implications. The trend of increasing sleep loss in children and the

potential impact on daytime functioning has been highlighted in several narrative reviews

published over the last decade (Buckhalt, Wolfson, & El-Sheikh, 2009; de Freitas Araújo

& Moraes de Almondes, 2014; Kopasz et al., 2010; Sadeh, 2007; Turnbull, Reid, &

Morton, 2013). For example, one review revealed that across all age groups, there has

been a decline in nightly sleep duration over the last 100 years (Matricciani, Olds, &

Petkov, 2011). Recent findings from the 2014 NSF Sleep in America poll revealed that

69% of children between the ages of 6 and 11 years were getting 9 h or more sleep per

night, 23% were getting approximately 8 h, and 8% were getting 7 h or less (NSF, 2014).

While it is thought that school-aged children should get approximately 10 h of sleep per

night, these recent statistics suggest that many children are not getting this amount of

sleep. Reduced sleep duration in children and adolescents has been largely associated

with use of electronic devices, including the use of social media (Cain & Gradisar, 2010).

Results from the NSF Sleep in America poll also showed that 75% of children had at

least one electronic device in their bedroom, and 51% of children had two or more

devices in their bedroom at night (NSF, 2014). Results from a recent meta-analysis

showed that social media device use was strongly associated with reduced sleep duration,

poorer sleep quality, and increased daytime sleepiness (Carter, Rees, Hale, Bhattacharjee,

& Paradkar, 2016). A recent study showed that adults who read with a light-emitting

electronic reader prior to bed had longer sleep onset latency (SOL), reduced melatonin secretion, delayed circadian clock, and were less sleepy before bed and less alert the next morning, as compared to those who read a printed book (Chang, Aeschbach, Duffy, & Czeisler, 2015).

Correlational Research on Sleep Restriction and Daytime Functioning in Children

The research literature on sleep restriction and the consequences for daytime functioning includes diverse outcomes, research designs, and methodology. To provide a global overview of the state of the literature on the impact of sleep loss on daytime functioning in children, meta-analyses were reviewed as these provide the strongest level of evidence (over individual studies). A comprehensive search of the literature was completed and six main meta-analyses were found; three of which included child/adolescent data (Astill, Van der Heijden, Van IJzendoorn, & Van Someren, 2012; Dewald, Meijer, Oort, Kerkhof, & Bögels, 2010; Lundahl, Kidwell, Van Dyk, & Nelson, 2015), and three which focused on adult data and are not included in the current review (Fortier-Brochu et al., 2012; Guo et al., 2013; Lim & Dinges, 2010).

The findings from Astill et al. (2012) and Dewald et al. (2010) were based primarily on correlational studies. These two meta-analyses reviewed a total of 106 unique studies (86 studies in Astill et al., 2012; 26 studies in Dewald et al., 2010; 6 studies reviewed in both). The focus of Astill et al. (2012) was on the relationship between sleep duration ($N = 24, 454$ participants) or sleep efficiency ($N = 1, 207$ participants), and cognitive functioning and behaviour. The focus of Dewald et al. (2010) was on the relationship between sleep duration ($N = 15, 199$ participants) or sleep quality ($N = 13, 631$ participants), and school performance. Results of the correlational reviews

collectively indicated that reduced sleep duration was associated with reduced cognitive

functioning and increased behavioural problems (Astill et al., 2012). Reduced sleep

duration was also associated with increased academic problems (Astill et al., 2012;

Dewald et al., 2010). Significant effect sizes for the relationships between school

performance and both sleep quality and sleepiness were found, indicating that better sleep

quality and less sleepiness were both associated with better school performance, although

these effect sizes were small (Dewald et al., 2010). Sleep efficiency was not significantly

associated with either cognitive performance or behavioural problems (Astill et al.,

2012). Taken together, the results from these reviews indicate that sleep amount is

significantly correlated with aspects of cognitive functioning (i.e., executive functioning,

multiple-domain cognition), and school performance, but not sustained attention or

memory (Astill et al., 2012). Of note, there was significant heterogeneity reported in the

reviews with respect to effect sizes among the studies within the reviews. This

heterogeneity was likely due to the broad range of outcomes that were assessed, such as

many aspects of cognitive functioning measured in multiple ways, and multiple, different

informants reporting on outcomes.

Experimental Research on Sleep Restriction and Daytime Functioning in Children

Lundahl et al. (2015) included only 13 studies in which children's and

adolescents' sleep was experimentally manipulated, and the primary outcomes of interest

were attention ($N = 268$ participants) and hyperactivity ($N = 171$ participants). In contrast

to the meta-analysis described above, results from Lundahl et al. (2015) suggested that

attention is significantly impacted by sleep restriction, although heterogeneity in effect

sizes across studies was noted. Ratings of hyperactivity/impulsivity were not significantly

different when measured during sleep restriction versus baseline sleep or extended sleep (Lundahl et al., 2015).

Astill et al. (2012) also included some studies where sleep was experimentally manipulated and this subset of studies was examined by way of moderator analyses. Results from one moderator analysis of four studies showed that there was a significant positive association between sleep duration and behaviour problems when the sleep manipulation was two or more nights. Results from another moderator analysis of 10 studies showed that in contrast to Lundahl et al. (2015) there was no significant association between sleep duration and cognitive problems (Astill et al., 2012).

While the Lundahl et al. (2015) review is recent, it was focused only on the relationship between sleep loss and attention and hyperactivity. To broaden the scope of daytime outcomes, a literature review was conducted and yielded 20 publications (representing 17 unique studies). Twelve of these studies were included in the meta-analysis by Lundahl and colleagues (2015). Eight studies (10 publications) involved school-aged children (Biggs et al., 2001; Fallone et al., 2001; Fallone et al., 2005; Gruber et al., 2011; Gruber et al., 2012; Peters et al., 2009; Randazzo et al., 1998; Sadeh, Gruber, & Raviv, 2003; Vriend et al., 2013; Poirier, Gendron, Vriend, Davidson, & Corkum, 2016), and eight studies (nine publications) involved adolescents (Baum et al., 2014; Beebe, DiFrancesco, Tlustos, McNally, & Holland, 2009; Beebe et al., 2008; Carskadon, Harvey, & Dement, 1981a; Carskadon, Harvey, & William, 1981b; Jiang et al., 2011; Kopasz et al., 2010; Louca & Short, 2014; Voderholzer et al., 2011). One additional study examined the effects of sleep restriction in adolescents and adults (Talbot, McGlinchey, Kaplan, Dahl, & Harvey, 2010). Results of the 10 papers with school-aged

children are discussed in the current review (See Table 2.1). The inclusion criterion was that the mean age of the children had to be between 6 and 12 years.

The eight child studies (yielding 10 publications and a total of 372 participants) collectively used varying designs (i.e., between-subjects, within-subjects, mixed design), a range of sleep manipulations (i.e., acute versus cumulative, sleep deprivation versus restriction), and a variety of data collection methods (e.g., questionnaires, direct measures, multiple informants). Half of the studies ($n = 4$) employed between-subjects designs, while three studies (five publications) used within-subjects designs. One study employed a mixed design as a group of children with ADHD was included as a comparison group to TD children (Gruber et al., 2011). This study is discussed in a separate section of this paper focused on sleep in children with ADHD (below). Six of the eight studies examined the impact of sleep restriction (one acute and five cumulative), and three studies (four publications) examined acute sleep deprivation.

Results from the three studies (five publications) that used within-subjects designs showed that sleep manipulations, restriction/deprivation, both cumulative and acute, were successful and participants consistently slept significantly less in the restricted condition compared to the optimized ($n = 2$) or extended conditions ($n = 1$). One study (with two publications) used acute sleep restriction of one night with TIB limited to 5 h compared to an optimized sleep with 10 h TIB (Biggs et al., 2010; Peters et al., 2009). One study compared cumulative sleep restriction of either 6.5 h or 8 h TIB for one week to one week of optimized sleep with 10 h TIB (Fallone et al., 2005). The final study (with two publications) employed a cumulative sleep restriction of 1 h less TIB per night for four

nights compared to optimized sleep of 1 h extra TIB for four nights (Poirier et al., 2016; Vriend et al., 2013).

The four studies that used between-subjects designs showed that sleep manipulations, restriction/deprivation, both cumulative and acute, were successful and participants consistently slept significantly less in the restricted condition compared to the optimized ($n = 2$) or extended conditions ($n = 2$). Two studies used cumulative sleep restriction of 1 h less TIB compared to 1 h extra TIB, one study for one week (Gruber et al., 2012), and one study for three nights (Sadeh et al., 2003). The other two studies with between-subjects designs both used acute sleep deprivation where they examined children following one night where TIB was reduced to 4 h (Fallone et al., 2001) or 5 h (Randazzo et al., 1998) compared to optimized sleep of 10 h TIB (Fallone et al., 2001) or 11 h TIB (Randazzo et al., 1998).

Impact of Sleep Restriction on Daytime Functioning

Attention. Results from the seven studies that included measures of attention showed that reduced sleep impacted both subjective and objective measures of attention (see Table 2.1). Two studies used subjective measures and found an impact on at least one measure of attention. Of the six studies that used objective measures, four found significant impacts on attention. Children were subjectively rated as having more attention problems following cumulative sleep restriction compared to extended sleep (Poirier et al., 2016), and when acutely sleep deprived compared to optimized sleep (Fallone et al., 2001).

Children had more difficulty on objective tasks assessing divided attention following a cumulative sleep restriction condition as compared to performance following

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an extended sleep condition (Vriend et al., 2013). Reaction times were significantly slower on a vigilance task, and children demonstrated significantly more lapses in attention after restricted sleep compared to optimized sleep (Peters et al., 2009). Children who experienced cumulative sleep restriction also performed worse on a simple reaction time task compared to their baseline performance (Sadeh et al., 2003). Interestingly, while some children who were sleep restricted showed no significant differences in reaction time on a continuous performance task, children who had extended their sleep significantly improved their reaction time scores compared to baseline performance (Sadeh et al., 2003). This indicates that while sleep restriction was not necessarily detrimental to performance, extended sleep seemed to be advantageous. Neither of the studies that examined acute sleep deprivation found that children with reduced sleep performed worse on objective attention measures compared to children with optimized sleep conditions (Randazzo et al., 1998; Fallone et al., 2001). Taken together, the findings from these seven studies suggest that attention is affected by sleep, however, it is not clear whether sleep restriction negatively affects attention, or whether optimized or extended sleep improves attention relative to baseline performance.

Emotion. Three studies examined emotional functioning following experimental sleep manipulation. All three studies used subjective measures of emotion, and one study also used an objective measure of emotion. Vriend et al. (2013) found that children demonstrated significantly less positive affect following sleep restriction compared to sleep extension based on an objective test of emotional response. There was no significant difference in negative affective response. Parents reported significantly worse emotional regulation after restricted sleep compared to extended sleep (Vriend et al.,

2013). Children did not self-report any significant difference in affect following restricted sleep compared to extended sleep. One study (Gruber et al., 2012) found that teachers' ratings of children following cumulative sleep restriction (i.e., 1 h less TIB/night for one week) had increased emotional lability compared to baseline. Further, children with extended sleep (i.e., 1 h extra TIB/night for one week) showed improved ratings compared to baseline (Gruber et al., 2012). On the other hand, Fallone et al. (2005) found no significant differences in teacher ratings of affect/mood following restricted sleep as compared to optimized sleep.

Cognitive (memory and academic). Four studies examined the impact of reduced sleep on objective measures of memory and one of the four studies found that memory was significantly impacted by shortened sleep (see Table 2.1). Results showed that short-term memory and working memory were significantly worse following cumulative sleep restriction compared to extended sleep (Vriend et al., 2013), whereas declarative memory was not significantly different between acutely restricted sleep and optimized sleep (Biggs et al., 2010). One study found that children who had cumulatively extended sleep (i.e., 1 h extra per night for three nights) had significantly better performance on a task assessing verbal memory compared to baseline performance. No significant differences were observed for children in the cumulative sleep restriction group (Sadeh et al., 2003). Similarly, Randazzo et al. (1998) found no significant differences in performance on a battery of memory tests when children were acutely sleep deprived (i.e., 5 h TIB) compared to having optimized sleep (i.e., 11 h TIB).

Two studies examined academic performance and results from one study showed that teachers reported more academic problems when children were sleep restricted

compared to having optimized sleep (Fallone et al., 2005). Furthermore, children who were acutely sleep deprived (i.e., 5 h TIB) demonstrated significantly more general errors on an abstract learning task compared to children who had optimized sleep (i.e., 11 h TIB). There were no significant differences between groups on objective measures of visual or verbal learning (Randazzo et al., 1998).

Summary of results from the experimental sleep studies in children. There has been slow but steady growth over the last 10 years in the use of experimental approaches to the study of sleep in TD children. Taken together, the results of the eight reviewed experimental sleep manipulation studies suggest regardless of experimental design (i.e., within- versus between-subjects), and type of sleep manipulation (restriction versus deprivation; acute versus cumulative), attention seems to be most consistently impacted by sleep. However, it is not clear whether attention is negatively affected by sleep restriction or improved by extended/optimized sleep. There is some evidence that behaviour and emotional functioning/affect are also affected by sleep loss, whereas effects on memory are less consistent. While variation existed, results also tended to demonstrate that cumulative sleep loss generally resulted in poorer performance than acute sleep loss. Furthermore, it is important to highlight that there was evidence to show that extending/optimizing sleep was beneficial such that in some cases where children did not show significant impairment following sleep restriction/deprivation, improvements relative to baseline were observed following sleep extension/optimization. The above findings are based on TD children only. These findings suggest that baseline sleep levels may be less than optimal for performance, and therefore extending sleep has beneficial effects.

Sleep and Mental Health in Children

Similar to the findings in the adult literature reviewed above, it is well documented that sleep problems are very common in children with mental health disorders, such as ADHD, anxiety, and depression (See Alfano & Gamble, 2009; Gregory & Sadeh, 2012 for comprehensive reviews on children's sleep and psychopathology). Based on subjective measures of sleep, children with depression or anxiety report three times the number of sleep problems compared to TD youth (Shanahan, Copeland, Angold, Bondy, & Costello, 2014). One study found that 50% of children with insomnia also met criteria for one or more mental health disorders, with 61% meeting criteria for ADHD, 65% meeting criteria for anxiety, and 30% meeting criteria for depression (Ivanenko, Barnes, Crabtree, & Gozal, 2004).

As in TD children, symptoms of insomnia are the most commonly reported sleep problems in children with mental health disorders (Hansen, Skirbekk, Oerbeck, Wentzel-Larsen, & Kristensen, 2013; Shanahan et al., 2014). The high rate of insomnia in children with mental health disorders is particularly concerning given that the evidence from TD children indicates that sleep loss causes significant impairment in daytime functioning. Children with mental health problems are already at higher risk for difficulties in the areas known to be impacted by poor sleep, such as attention, emotional regulation, cognition (e.g., memory), and academic performance. In particular, research shows that attention is consistently affected by sleep loss, as demonstrated by the findings from experimental sleep manipulation studies (Table 2.1).

Sleep and ADHD

The prevalence of ADHD in school-aged children is estimated to be approximately 5-7% (Wilcutt, 2012). Of those children, the co-occurrence of sleep problems is reported to be anywhere from 25-50% (Owens, 2005; Spruyt & Gozal, 2011; Yoon, Jain, & Shapiro, 2012). In fact, in an earlier version of the Diagnostic and Statistical Manual for Mental Disorders (DSM-III), sleep problems were included in the diagnostic criteria for ADHD. Much research has been dedicated to the relationship between sleep and ADHD in children. Several narrative reviews (e.g., Corkum, Davidson, Tan-MacNeill, & Weiss, 2014; Jan, Yang, & Huang, 2011; Konofal, Lecendreux, & Cortese, 2010; Spruyt & Gozal, 2011; Yoon et al., 2012), and quantitative reviews (e.g., Cortese, Faraone, Konofal, & Lecendreux, 2009; Cortese, Konofal, Yateman, Mouren, & Lecendreux, 2006; Sadeh, Pergamin, & Bar-Haim, 2006), as well as one review of reviews (Corkum & Coulombe, 2013), have been published.

Corkum and Coulombe's summative review of all published quantitative reviews revealed that taken together, results from the three meta-analyses (Cortese et al., 2009, Cortese et al., 2006; Sadeh et al., 2006) were consistent in showing that parents of children with ADHD reported significantly more sleep problems on subjective measures of sleep (e.g., questionnaires) compared to parents of TD children. The findings from objective measures of sleep (i.e., actigraphy, polysomnography) showed that there were many inconsistencies in the literature around sleep duration in children with ADHD versus TD children. While Cortese et al. (2009) concluded that children with ADHD had significantly shorter sleep durations (as measured by actigraphy), another review concluded that sleep durations (as measured by PSG) were comparable between children

with ADHD and TD children (Sadeh et al., 2006). Sleep onset latency at bedtime was comparable between TD and ADHD groups in two of the three reviews (Cortese et al., 2009; Cortese et al., 2006). Results from one review, where actigraphy was analyzed separately from PSG, revealed that children with ADHD had longer SOL than TD children (Cortese et al., 2009). All three reviews consistently reported that ADHD and TD groups did not differ in their sleep architecture (Cortese et al., 2009; Cortese et al., 2006; Sadeh et al., 2006). Both reviews that included results from daytime nap opportunities (i.e., Multiple Sleep Latency Tests [MSLTs]) showed that despite no difference in SOL at night, children with ADHD had significantly shorter SOL during MSLT nap opportunities, indicating more daytime sleepiness than TD peers (Cortese et al., 2009; Cortese et al., 2006).

A more recent meta-analysis that examined sleep (as measured by actigraphy) in children with ADHD found that sleep duration was not significantly different between children with ADHD and TD controls; however, SOL was found to be significantly longer in children with ADHD (De Crescenzo et al., 2016). It is important to consider that while actigraphy is able to provide valid estimates of sleep variables for TD children, and children with ADHD while on medication, there is some evidence that actigraphy may underestimate sleep variables (relative to polysomnography) for children with ADHD who are not taking medication (Waldon et al., 2016).

Overall the results from these reviews are quite variable. While results showed that parents of children with ADHD report more sleep problems (mostly consistent with insomnia) than parents of TD children, the same findings have not been consistently found using objective measures. This variability is likely due to different modes of

measurement of sleep variables (i.e., actigraphy versus PSG), and the fact that among these three reviews, one separated data from PSG and actigraphy, one reported on PSG and actigraphy together, and one review only included studies with PSG data.

Daytime Functioning and Sleep Problems in Children with ADHD

It is well established that children with ADHD have increased difficulty across multiple domains of daytime functioning as compared to their TD peers. Children with ADHD have more difficulty than TD peers on both subjective ratings and objectively measured tasks assessing attention (Berger, Slobodin, & Cassuto, 2017; Mullane, Corkum, Klein, McLaughlin, & Lawrence, 2011; Negut, Jurma, & David, 2016; Waldon, Vriend, Davidson, & Corkum, 2015), working memory (Davidson, Cherry, & Corkum, 2015; Simone, Bédard, Marks, & Halperin, 2016; Sowerby, Seal, & Tripp, 2011), and alertness (Gruber & Sadeh, 2004). Given these difficulties, combined with the knowledge that insufficient sleep and daytime sleepiness have negative impacts on otherwise healthy children in some or perhaps all of these areas, it is very likely that children with ADHD may be even more negatively impacted by insufficient sleep.

There are very few published studies examining the daytime impacts of sleep restriction/deprivation on children with ADHD. One such correlational study found that children aged 10-14 years with ADHD who reported high levels of daytime sleepiness were more likely to be rated by their parents as having academic impairment and by their teachers as having poor academic competence, even after controlling for symptoms of ADHD (Langberg, Dvorsky, Marshall, & Evans, 2013). In another study of children with ADHD, total sleep time (TST), as measured by actigraphy, was not correlated with performance on an objective measure of attention (continuous performance task [CPT]);

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however, low sleep efficiency was associated with more variable reaction times (Moreau, Rouleau, & Morin, 2013). Additionally, TST was significantly correlated with parent reported difficulties across several executive functioning domains (Moreau et al., 2013).

It is important to note that there is only one study to date that has assessed daytime functioning following experimental sleep manipulation in both TD children and children with ADHD (Gruber et al., 2011). Results revealed that all children in the study ($n = 43$) demonstrated significantly more difficulty on a vigilance task (CPT) following sleep restriction, with more omission errors (indicating more inattention), fewer commission errors (indicating less impulsivity), and generally slower reaction times. However, children with ADHD ($n = 11$) generally had more omission errors than their TD peers at baseline and following sleep restriction, and only the children with ADHD had scores in the clinical range following sleep restriction (Gruber et al., 2011). This study included a small number of children with ADHD, so the reliability of the findings needs to be confirmed in larger studies.

Stimulant Medication and Sleep

Another important consideration in understanding the relationship between ADHD and sleep is examining the impact of stimulant medications. Results from a Canadian survey revealed that the use of stimulant medication in children with ADHD increased from 43.4% in 2000 to 59.3% in 2007 (Brault & Lacourse, 2012), and it is likely that this trend has continued since 2007. It is well documented that while stimulant medications improve daytime functioning in children with ADHD (Faraone & Buitelaar, 2010), they also have a negative impact on sleep, such as longer SOL, reduced sleep duration, and reduced sleep efficiency (Corkum, Panton, Ironside, MacPherson, &

Williams, 2008; Galland, Tripp, & Taylor, 2010; Mick, Biederman, Jetton, & Faraone, 2010). Given the relationship between stimulant medications and negative sleep side-effects, in combination with the relationship between pre-existing sleep problems in children with ADHD and the impact of insufficient sleep on daytime functioning in children, it is important for clinicians to carefully monitor sleep when prescribing stimulant medications for children with ADHD.

Conclusions

Sleep is important for healthy daytime functioning, and while results differ depending on methodology and measurement (e.g., objective versus subjective), it is clear that children who do not have optimal sleep are at risk for daytime difficulties. Based on both correlational and experimental research, sleep duration seems to affect attention, emotional functioning, and cognitive functioning, however more evidence is needed to determine whether it is sleep restriction that is impairing, or extended/optimized sleep that is improving these daytime functions relative to baseline performance. It is important to note that these findings are based on TD children who have experienced only mild sleep restriction/deprivation. The effect of cumulative sleep restriction over time (i.e., months or years) may result in even more widespread negative daytime consequences. Furthermore, the impact of insufficient sleep on children with ADHD (or children with other mental health disorders) has not yet been well established; however, it is hypothesized that effects will be even greater than in TD children. In summary, there is evidence to suggest that sleep plays a role in healthy daytime functioning, and more research is necessary to better understand this complex relationship in TD children, as well as in children with mental health disorders.

Table 2. 1

Summary of Studies with Experimental Manipulation of Sleep in School-Aged Children

First Author, Year	Population	Design	Outcomes	Main Findings
Biggs et al., 2010	$N = 14$ (all F) Mean age = 10.6y TD	Within-subjects Lab-based sleep data collection Acute sleep deprivation = 5 h TIB for 1 night Compared to optimized sleep = 10 h TIB for 1 night	Sleep *Subjective*: - Parent & child sleep diary *Objective*: - Actigraphy Daytime Functioning *Objective:* Biggs et al., 2010: - Declarative memory (Auditory Verbal Learning Test) Peters et al., 2009: - Psychomotor vigilance task (PVT- measures reaction time and number of lapses)	Sleep: - Manipulation successful: mean time in bed and sleep latency were both reduced, and mean sleep efficiency was higher on the sleep deprivation night compared to optimized sleep Daytime Functioning: Biggs et al., 2010: - No significant differences between sleep deprivation night and optimized sleep for acquisition of word lists (memory) - No significant effect of condition or interaction was found for delayed recall of word lists Peters et al., 2009: - Significant main effect of condition and time of day were found for PVT reaction times - Reaction times were significantly longer following sleep deprivation night when tested at 07:30 and 09:30 compared to optimized - Significant main effect of time of day on lapses - Sleep deprived condition showed significant increase in lapses at 07:30 and 09:30 - No significant differences in optimized sleep condition

First Author, Year	Population	Design	Outcomes	Main Findings
Peters et al., 2009 *Same study as Biggs et al., 2010	*N* = 14 (all F) Mean age = 10.6y TD	Within-subjects Lab-based sleep data collection Acute sleep deprivation = 5 h TIB for 1 night Compared to optimized sleep = 10 h TIB for 1 night	Sleep *Subjective*: - Parent & child sleep diary *Objective*: - Actigraphy Daytime Functioning - Psychomotor vigilance task (PVT- measures reaction time and number of lapses)	Sleep - Significantly shorter sleep duration during sleep deprivation Daytime Functioning - Significant main effect of condition and time of day were found for PVT reaction times - Reaction times were significantly longer following sleep deprivation night when tested at 7:30am and 9:30am compared to optimized - Significant main effect of time of day on lapses - Sleep deprived condition showed significant increase in lapses at 07:30 and 09:30 - No significant differences in optimized sleep condition

Fallone et al., 2005	*N* = 74 (39 M)
	Range: 6.5-12.9 y
	Mean age = 10.1y
	
	TD children
		Within-subjects
		
		Home-based sleep data collection
		
		Cumulative sleep deprivation = 8 h TIB for grades 1&2; 6.5 h TIB for Grade 3 and above for 4-6 nights
		
		Compared to optimized sleep = 10 h
			Sleep
			Subjective:
			- Sleep Diary
			- Sleepiness item
			
			Objective:
			- Actigraphy
			
			Daytime Functioning
			Subjective:
			School Situations Questionnaire (SSQ):
			- problem behaviour in school setting
			
			Author made questionnaire
				Sleep
				- Optimized sleep was on average 43 min TIB more than baseline
				- Deprived sleep was 165 min TIB less than baseline
				
				- Sleepiness was significantly higher in both deprived and optimized compared to baseline, but deprived and optimized did not significantly differ
				
				Daytime Functioning
				- Main effect of condition on:
				  - Academic problems
				  - School Situations total problems and severity of problems

First Author, Year	Population	Design	Outcomes	Main Findings
		TIB for 4-6 nights and baseline sleep	assessing 4 areas: - Academic problems - Hyperactive/impulsive behaviour - Internalizing symptoms - Opposition/aggression - Sleepiness	- Sleepiness item - Follow up comparisons showed: - More academic problems when sleep deprived compared to Optimized and baseline - SSQ total problems higher when sleep deprived and optimized sleep compared to baseline, but not significantly different between conditions - SSQ mean severity significantly higher when sleep deprived compared to baseline, but not compared to optimized sleep
Fallone et al., 2001	*N* = 87 (46 M) Range: 8.6-15.8 y Mean age: 11.9 y	Between-subjects Lab-based sleep data collection Acute sleep deprivation = 4 h TIB for 1 night Compared to optimized sleep = 10 h TIB for 1 night	Sleep/Sleepiness *Subjective:* - Sleep diary - Sleepiness ratings *Objective*: - Actigraphy - PSG - MSLT Daytime Functioning *Subjective*: - ADHD symptoms - Behaviour *Objective*: - Sustained Attention - Response inhibition	Sleep - Manipulation successful, children in restricted condition slept significantly less - MSLT showed shorter SOL for children with restricted sleep Daytime Functioning *Subjective*: - Children in sleep restricted group rated as more inattentive and displayed more sleepy behaviours *Objective*: - No significant difference on performance on tasks of response inhibition and sustained attention

First Author, Year	Population	Design	Outcomes	Main Findings
Gruber et al., 2012	$N = 34$ (20 M) Range: 7-11 y Mean age: 8.5 y TD children	Between-subjects Home-based sleep data collection Cumulative sleep restriction = 1 h less TIB for 5 nights Compared to extended sleep = 1 h more TIB for 5 nights	Sleep/Sleepiness *Subjective*: - Epworth sleepiness scale *Objective*: - actigraphy Daytime Functioning *Subjective (Teacher):* - Emotional lability - Restless/Impulsive behaviour	Sleep/Sleepiness - Based on actigraphy, children were sleeping longer in Sleep Extended group and shorter in Sleep Restricted group - Children were sleepier in the Sleep Restriction group compared to baseline, children were less sleepy in the Sleep Extension group compared to baseline Daytime Functioning - Emotional lability and restless-impulsive behaviours improved from baseline for the sleep extended group, whereas scores worsened for the sleep restricted group
Randazzo et al., 1998	$N = 16$ (7 M) Range: 10-14 y Mean age: 11.6 y TD children	Between-subjects Lab-based sleep data collection Acute sleep deprivation = 5 h TIB for 1 night Compared to optimized sleep = 11 h TIB for 1 night	Sleep *Objective:* - PSG - MSLT Daytime Functioning *Objective:* - Abstract thinking - Memory (WRAML) - Learning (CCT task) - Creativity - Psychomotor vigilance/alertness (Digit Symbol Substitution Test [DSST] – timed coding task assessing attention	Sleep - Mean sleep duration was significantly reduced for sleep deprived group - Sleep efficiency was significantly higher for sleep deprived group - Based on MSLT, sleepiness increased for sleep deprived group -Psychomotor vigilance/alertness: - DSST: - Significant main effect of time - No main effect of sleep condition - Time by group interaction where sleep deprived group

First Author, Year	Population	Design	Outcomes	Main Findings
			and reaction time & Steer Clear task – computerized task of driving a car and avoiding cows on a road)	improved on DSST over time, but not to the same degree as the optimized group – this was observed at the 12:45 testing session - No significant difference on the Steer Clear task between groups Cognitive: -Sleep deprived group performed significantly worse on tasks of verbal creativity - No significant difference on the CCT (learning and problem solving) - No significant difference on the WRAML or CVLT
Sadeh et al., 2003	*N* = 72 (39 M) Range: 9.1-12.2 y Mean age = 10.6 y TD children	Between-subjects Home-based sleep data collection Cumulative sleep restriction = 1 h less TIB for 3 nights Compared to extended sleep = 1 h more TIB for 3 nights Created three groups out of the manipulation: Sleep restriction group, sleep	Sleep *Subjective:* - Sleep diaries *Objective:* - Actigraphy Daytime Functioning *Objective:* - Motor speed (finger tapping test) - Vigilance/RT - Sustained attention (CPT) - Visual scanning (simple digit substitution task) - Visual memory (visual digit span test) - Learning task (serial digit learning test)	Sleep - Sleep onset time, sleep period, true sleep time, sleep percent, night waking and quiet sleep were all significantly different for children in the restricted sleep group - Several subjective measures were also significantly different for groups (evening fatigue, predicted sleep latency, reported sleep latency) - Differences in sleep variables were also found by gender Daytime Functioning - Significant group by period interactions for simple reaction time, digit forward, and reaction time on CPT - Children who extended sleep had significant better performance on the digit

First Author, Year	Population	Design	Outcomes	Main Findings
		extension group, and no change group Data analyzed between three groups and performance from baseline to post-manipulation		forward memory task between and post-intervention - Only sleep extended group had significantly better performances on the CPT-RT. Children in sleep restriction group or no change group showed no significant differences - On the simple reaction time test, children who were sleep restricted and no change group performed significantly worse whereas sleep extended group showed no difference
Vriend et al., 2013	*N* = 32 (14 M) Range: 8-12 y Mean age = 9.8 y TD children	Home-based sleep data collection Cumulative sleep restriction = 1 h less TIB for 4 nights Compared to extended sleep = 1 h more TIB for 4 nights	Sleep *Subjective:* - Sleep Diary - Pictorial Sleepiness Scale *Objective:* - Actigraphy Daytime Functioning *Subjective*: - Parent and child emotion questionnaires - Parent rated attention *Objective*: - Affective Response Task - Short term memory - Working memory - attention (ANT-I; Children's Colour Trails Test [CCTT] 1 & 2)	Sleep - Sleep manipulation worked, restricted sleep was 145.6 min shorter than extended sleep Daytime Functioning - Overall emotional functioning was significantly impacted by sleep restriction - Specifically less positive affective response and poorer parent reported emotion regulation - No significant difference in child rated emotion or negative affective response - Significant differences in performances on short term memory, working memory, math fluency, (reduced performance) and parent reported inattention (increased symptoms), and CCTT-2 - No significant differences in ANT-I tasks or CCTT-1

First Author, Year	Population	Design	Outcomes	Main Findings
			- Math Fluency	-Some order effects were noted in that performance was impacted depending on which condition was experienced first (working memory, controlling emotions)
Poirier et al., 2016 *Same study as Vriend et al., 2013	*N* = 25 (12 M) Range: 8-12 y Mean age: 9.72 y TD children	Home-based sleep data collection Cumulative sleep restriction = 1 h less TIB for 4 nights Compared to extended sleep = 1 h more TIB for 4 nights	Sleep *Subjective:* - Sleep Diary - Pictorial Sleepiness Scale *Objective:* - Actigraphy Daytime Functioning *Subjective*: - Parent reported ADHD symptoms - RA reported ADHD symptoms *Objective*: - Daytime activity (actigraphy)	Sleep - Participants slept significantly longer during extended sleep than restricted sleep Daytime Functioning *Subjective*: - Parents reported increased inattention during restricted sleep - RAs did not report significantly different symptoms when sleep restricted *Objective*: - No significant differences in daytime activity levels
ADHD				

Gruber et al., 2011	*N* = 43 (27 M)
	Range: 7-11y
	Mean age = 8.7 y
	
	TD and ADHD
	N = 34 TD
	N = 11 ADHD
		Mixed Between-/within-subjects
		
		Home-based sleep data collection
		
		Cumulative sleep restriction = 1 h less TIB for 6 nights
		
		Compared to
			Sleep
			Subjective:
			- Sleep diary
			- Epworth sleepiness scale
			
			Objective:
			- Actigraphy
			- 1 night at home PSG
			
			Daytime Functioning
			Subjective:
			- Internalizing symptoms
				Sleep
				When sleep restricted compared to baseline sleep, children had:
				  - Shorter sleep duration
				  - Shorter sleep onset latency
				  - Higher sleep efficiency
				  - Decreased fragmentation
				  - Increased sleepiness
				
				Daytime Functioning
				Both TD and ADHD children demonstrated:

First Author, Year	Population	Design	Outcomes	Main Findings
		baseline sleep	- Externalizing symptoms - Emotional problems - Attention - H/I behaviours *Objective:* - Vigilance/RT (CPT)	- More omission errors - Fewer commission errors - Slower reaction times when sleep restricted compared to normal sleep - Children with ADHD generally had more omission errors than TD

Note. F = female; M = males; y = years; TD = typically developing; TIB = time in bed; h = hour(s); min = minutes; RA = research assistant; RT = reaction time; PSG = polysomnography; MSLT = multiple sleep latency test; SOL = sleep onset latency.

Chapter 3: Impact of Sleep Restriction on Attention, Emotions, and Cognitive

Functioning in Children with ADHD and their Typically Developing Peers

The manuscript based on this experimental study is presented below. This study is part of a larger study examining the effects of sleep restriction on children generally. The focus of this study was on the impact of sleep restriction on daytime functioning. Readers are advised that Fiona Davidson, under the supervision of Dr. Penny Corkum, participated in the initial conceptualization of the research study, helped to develop the study protocol and prepared submissions for ethical review, was responsible for recruitment, completed and oversaw data collection, scoring, data checking, and data analysis/interpretation for all measures included in this study. Fiona Davidson also applied for and was successful in obtaining funding to support this research. All aspects of this research were done in consultation with the dissertation committee (Dr. Benjamin Rusak and Dr. Christine Chambers). Fiona Davidson was responsible for all aspects of the writing process, and received editorial feedback from dissertation committee members.

Abstract

Correlational studies show that sleep loss is associated with negative daytime outcomes in school-aged children, yet few experimental sleep manipulation studies exist. Therefore, causal relationships cannot be determined. A sample of age and sex matched children with attention-deficit/hyperactivity disorder (ADHD; $n = 18$) and typically developing (TD) children ($n = 18$) participated in a mild cumulative experimental sleep manipulation consisting of a Restricted sleep condition (1 h less time in bed [TIB] per night for six nights) and a Typical sleep condition (six nights of controlled habitual sleep). Impact on children's daytime functioning was examined following each condition. At baseline, both groups were sleeping the recommended amount for their age group (i.e., ~10 h TIB/night). Children successfully reduced TIB by ~1 h, however total sleep time (TST) was reduced by only ~20 min, due to children falling asleep faster and spending less time awake after sleep initiation during the Restricted condition compared to Typical condition. Despite the limited sleep restriction, both TD children and children with ADHD demonstrated significant differences in performance on an objective attention task and on subjective reports of emotional lability after sleep restriction. There was no differential impact on children with ADHD. Results suggest that mild sleep restriction (~20 min/night for six nights) can affect children's attention and emotional regulation. These results have consequences for children's learning and behaviour during this critical developmental period.

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Introduction

The daytime consequences of sleep restriction and deprivation in adults have received much research attention, and the pediatric literature around sleep restriction is growing (Mindell et al., 2011). Correlational research provides evidence for relationships between shorter sleep duration and daytime functioning problems including cognitive functioning (Buckhalt, El-Sheikh, Keller, & Kelly, 2009; Cho et al., 2015; Gruber et al., 2010; Paavonen et al., 2010), and academic performance (Wolfson & Carskadon, 1998). While experimental manipulation of sleep duration is necessary to demonstrate that sleep duration affects cognitive and emotional functioning, few such studies are currently available.

There are currently eight studies (10 publications) that have experimentally manipulated sleep and assessed daytime functioning in school-aged children (Biggs et al., 2010; Fallone et al., 2001; Fallone et al., 2005; Gruber et al., 2011; Gruber et al., 2012; Randazzo et al., 1998; Sadeh, Gruber, & Raviv, 2003; Vriend et al., 2013). Across these eight studies, different methods were used to restrict sleep (i.e., cumulative sleep restriction [$n = 5$] versus acute sleep deprivation [$n = 3$]), study design (i.e., within-subjects [$n = 3$], between-subjects [$n = 4$], mixed [$n = 1$]), and comparison condition (i.e., extended [$n = 3$], optimized [$n = 4$], or baseline [$n = 1$] sleep). Different outcome measures were also used to assess daytime functioning (e.g., attention, emotions, academic performance, behaviour) with a mix of subjective (i.e., questionnaires) and objective (i.e., direct, performance-based) measures. The results of these studies are inconsistent, making it difficult to draw firm conclusions. Overall there is some evidence to suggest that even a mild cumulative sleep restriction (e.g., 1 h over a few days) can

significantly affect daytime functioning in typically developing (TD) children. These findings are particularly important because mild, cumulative sleep loss is a more common and enduring problem in children than a single night of substantial or complete sleep loss.

Of the five experimental sleep manipulation studies that examined cumulative sleep restriction, all assessed the impact on attention, two with objective measures, two with subjective measures, and one with both objective and subjective measures. These studies found that objectively measured attention is significantly different between restricted sleep and extended sleep conditions (Vriend et al., 2013), and between restricted sleep and baseline sleep (Gruber et al., 2011, Sadeh et al., 2003). The two studies that used subjective measures of attention found significant differences between restricted sleep and optimized (Fallone et al., 2005) or extended sleep (Vriend et al., 2013). Taken together, every study measuring attention found a difference on at least one measure.

Three of the studies examined emotional functioning following sleep manipulation. Only one of these studies used an objective measure of emotion, and results showed significant differences between restricted and extended sleep conditions (Vriend et al., 2013). With respect to subjective measures, one study measured parent-rated emotional functioning and found that subjective ratings were significantly different between restricted and extended sleep (Vriend et al., 2013). However, child self-reports were not significantly different (Vriend et al., 2013). Results for teacher ratings of emotional functioning were mixed. One study found significantly different ratings between restricted and extended sleep (Gruber et al., 2012), while Fallone et al. (2005)

did not observe significant differences in teacher ratings between restricted and optimized sleep conditions.

Two of the five studies using cumulative sleep restriction examined cognitive or academic functioning. One study found that performance on objectively assessed memory was significantly different between restricted and extended sleep conditions (Vriend et al., 2013), whereas the other study found no significant differences between restricted sleep and baseline sleep (Sadeh et al., 2003). Another study examined subjective ratings of academic work and found that ratings were significantly different between restricted and optimized sleep conditions (Fallone et al., 2005).

The impact of sleep restriction on TD children's daytime functioning (i.e., attention problems, difficulties regulating emotion, cognitive functioning difficulties) resembles the core symptoms of attention-deficit/hyperactivity disorder (ADHD), which include difficulties with attention and/or hyperactivity/impulsivity, and associated symptoms (i.e., emotional dysregulation, cognitive problems). The prevalence of sleep problems in children with ADHD has been estimated to be between 25-50%, with some reports as high as 95% (Corkum, Tannock, & Moldofsky, 1998; Owens, 2005; Spruyt & Gozal, 2011; Yoon, Jain, & Shapiro, 2012). Given that sleep loss affects attention and behaviour, and difficulties with attention and behaviour characterize ADHD, it is not surprising that the literature suggests a link between sleep and ADHD (Gruber, 2009). There has been very little research examining the impact of sleep restriction in children with ADHD. They may be more vulnerable than TD children given that they are predisposed to difficulty with daytime functions such as attention, and that they are reportedly more likely to have sleep problems than their TD peers. The only experimental

study of sleep loss that included children with ADHD evaluated the effects of mild sleep restriction on them relative to effects on TD controls using the Conners' Continuous Performance Task (CPT; Gruber et al., 2011). Children's sleep was restricted by 1 h per night for 6 consecutive nights and performance on the CPT was assessed once at the end of a baseline week and once following the sleep restriction week. Results showed that both children with ADHD and TD children demonstrated worse performance on the CPT when sleep was restricted compared to baseline. Although children with ADHD were not more negatively impacted by sleep restriction than the TD group (i.e., there was no group by condition interaction), their decline in performance on measures of inattention (i.e., omission errors, hit reaction time [hit RT]) moved them from the subclinical range at baseline, to the clinical range following sleep restriction.

The results of this first experimental sleep manipulation study which included both TD children and children with ADHD are limited by the narrow focus of the study, and the small sample size for the ADHD group ($n = 11$). Behaviour and sleepiness were assessed using only subjective parental reports, and neurobehavioural functioning was assessed only by the CPT task. Despite these limitations, this study highlights the possibility that sleep restriction may have clinically significant effects on children with ADHD, and further exploration is warranted.

In summary, there is some evidence in the pediatric sleep literature that TD children are significantly negatively impacted by reduced sleep duration across many different areas of daytime functioning when compared to optimized or extended sleep. Very little is known about the impact of sleep restriction on daytime functioning compared to children's typical sleep. Additionally, the impact of sleep restriction on

children with ADHD is largely unknown, given that only one study has explored this relationship. Therefore, the current study used a combined within- and between-subjects design to examine several aspects of daytime functioning in children with ADHD and TD controls following a mild, cumulative experimental sleep restriction compared to Typical sleep.

Research Hypotheses

1. Based on previous experimental sleep manipulation research, the first hypothesis was that both groups would demonstrate more daytime functioning difficulties with attention, emotions, and cognitive functioning on both subjective and objective measures in response to Restricted sleep as compared to Typical sleep.

2. The second hypothesis was that children with ADHD would be even more negatively impacted than TD children, resulting in poorer performance on both subjective ratings and objective measures of attention, emotions, and cognitive functioning.

<center>**Method**</center>

Participants

Both TD children and children diagnosed with ADHD aged 6-12 years were recruited for this study. Given that past research has found differences in sleep based on sex for post- but not pre-pubertal children (Carskadon et al., 2002; Fredriksen, Rhodes, Reddy, & Way, 2004), all participants were screened to ensure that they were pre-pubertal. Children were excluded from the study if they had a chronic and impairing medical illness (e.g., diabetes), history of neurological impairments (e.g., epilepsy), a primary sleep disorder (e.g., sleep apnea, periodic limb movement disorder), had used medication likely to affect sleep during the past month, had crossed more than two time

zones in the last month, regularly slept fewer than 8 h or more than 12 h nightly, and/or if they napped regularly.

Children in the TD group were recruited from the community through web-based advertisements, newsletters, as well as through a research database. Children participating in the TD group were screened to confirm that they had not been previously diagnosed with a mental health disorder and this was confirmed by screening questionnaires. Children in the ADHD group had a diagnosis of ADHD and were medication-naïve. Children with ADHD were excluded if they had a comorbid diagnosis of another primary mental health disorder such as major depression or generalized anxiety disorder, given that these disorders are also associated with sleep problems (Gregory & Sadeh, 2012). Children with ADHD were not excluded for having a learning disability given the high rates of learning disabilities in this population (~ 45%; DuPaul, Gormley, & Laracy, 2013). All children with ADHD were rigorously diagnosed by ADHD specialists (i.e., psychologists, developmental pediatricians) who use stringent diagnostic processes focusing on differential diagnoses. All assessments of ADHD included full psychoeducational assessments, parent and teacher diagnostic semi-structured interviews, observations, and questionnaires (see McGonnell et al., 2009 for detailed description of diagnostic procedures).

Of the 65 participants who met screening criteria (32 ADHD; 33 TD), 59 completed baseline (27 ADHD, 32 TD). After baseline, four children (2 ADHD; 2 TD) were excluded due to late stage exclusionary criteria: evidence of epileptic activity found on PSG ($n = 1$); could not confirm ADHD diagnosis ($n = 1$); change in pubertal status ($n = 2$). In addition, two participants from the ADHD group voluntarily withdrew from the

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study during the experimental sleep manipulation phase due to scheduling difficulties. In total, 53 children (23 ADHD, 30 TD) completed the entire sleep manipulation protocol. One participant from the TD group was excluded after completing the entire experimental protocol due to a diagnosis of diabetes after study completion. Of the remaining 52 children who participated, data were analyzed for 36 participants (18 ADHD; 18 TD) due to failure to meet minimal requirements for sleep restriction and group matching procedures for age and sex (see Results section).

Procedure

Following recruitment, each interested family completed a screening questionnaire based on inclusion/exclusion criteria to ensure that the child reached study criteria for participating in either the TD or the ADHD group. If these criteria were met, parents completed additional questionnaires that screened for primary sleep problems, mental health problems, and pubertal stage. If criteria were met, a meeting was scheduled and parental consent and child assent were obtained and the sleep lab visit schedule was developed.

This study employed a within- and between- subjects design to evaluate the impact of cumulative experimental sleep restriction (i.e., 1 h less TIB each night for six nights) on measures of attention, emotion, and cognitive functioning. Sleep restriction was achieved by scheduling bedtime 1 h later than normal while keeping wake time consistent across all study weeks. Participants attended a testing session at the end of each study phase (i.e., Baseline, Restricted, Typical).

All participants were provided with an actigraph and daily sleep diaries for at-home sleep data collection. Participants were instructed to wear the actigraph 24 h a day

(to record nocturnal sleep and ensure participants were not napping), and parents were asked to complete the sleep diary. During the two baseline weeks, children were instructed to follow their usual sleep and wake schedule. At the end of the second baseline week, participants and their parents went to the sleep lab for the first testing session. Families arrived at the lab 3 h prior to bedtime. The testing session included an overnight polysomnography (PSG) assessment which served as a final screening to ensure that participants did not have any primary sleep disorders and as an adaptation night for the child and family members to become familiar with procedures involved in PSG assessments.

The day following the overnight visit, a multiple sleep latency test (MSLT) protocol was completed. The MSLT protocol involved four nap opportunities during the day at 10:00, 12:00, 14:00, and 16:00 (see Measures section for more detailed description). Daytime functioning was also assessed during the day after the PSG assessment. Participants were provided with breakfast upon waking up and then had some of the PSG equipment removed. The daytime functioning assessment was divided into two sessions. All daytime functioning assessments were administered by a research assistant (RA) in the child bedroom portion of the sleep lab. The first session took place after the child had eaten breakfast and prior to the first MSLT nap opportunity. It included objective measures of attention, emotion, and cognitive functioning. Following the first session, the child was prepared for the first MSLT. After the first MSLT, the child had a small snack and the second testing session took place. The second session consisted of subjective, paper-and-pencil measures of sleep, attention, emotion, and cognitive functioning. After the second testing session, participants completed the second

MSLT, followed by lunch and free time (within the hospital), followed by the third MSLT, leisure time in the sleep lab, and finally the fourth MSLT. Child reports of sleepiness were recorded over the course of the testing day. Subjective, paper-and-pencil measures of children's sleepiness, attention, emotion, and cognitive functioning were completed by the RA directly after the testing session. Parent and teacher subjective reports of the child's functioning (e.g., sleep, sleepiness, attention, emotions, behaviour) were collected electronically at the end of each study week. Children and parents went home after the MSLT equipment was removed following the fourth and final nap. Both teachers and RAs were blind to experimental sleep condition, and RAs were blind to participants' diagnostic group.

Following baseline, actigraphy data were scored using relevant information from the sleep diary. Baseline data were used to calculate average sleep duration in a typical, habitual week for each participant. Efforts were made to ensure that the baseline weeks represented the typical sleep pattern for each individual (i.e., children followed their typical routines and bedtimes). These efforts included asking parents to indicate on the sleep diary whether or not each night of sleep was representative of the child's usual sleep habits. Using these data, two different sleep schedules were created: one that required a 1 h reduction of TIB for one week (Restricted condition), and one that required participants to adhere to a controlled typical sleep routine for one week (Typical condition), which was determined from their baseline weeks. Wake times remained unchanged throughout the study.

The order of the Restricted and Typical conditions was counterbalanced and there was a two-week recovery period between the two manipulation conditions in order to

eliminate any carryover effects. This recovery period was thought to be sufficient, given

that a past study found children required only one night of recovery sleep after one night

of total sleep deprivation (Carskadon et al., 1981a). The nights of sleep manipulation

were Sunday through Friday or Monday through Saturday nights (depending on sleep lab

availability). Participants returned to the sleep lab for testing sessions following the

Restricted condition and Typical condition (on Friday or Saturday). Daytime functioning

test sessions during manipulation weeks were identical to those during baseline.

Families were compensated with $75 for each overnight stay, and $25 for each

daytime testing session (for a total of $100 per condition). Therefore, the total

honorarium per participant was $300 plus a $75 completion bonus for completing all

parts of the study. Child participants were provided with a $15 gift card (e.g., movie

theatre, Subway) after each session, plus $1 prizes and stickers for completing the

daytime measures. Additional funds were provided to cover travel expenses (i.e., $10 per

trip for local participants and $25 per trip for those not local to the hospital setting).

Participants were also compensated for minor incidental expenses (parking, meals)

associated with visits to the sleep lab. All listed dollar amounts were provided in

Canadian dollars.

Finally, as an additional incentive, families in the ADHD group were provided the

opportunity for children to participate in a second research study, which included a

stimulant medication trial following the experimental sleep study. Benefits to

participating in the medication trial included: 1) access to a highly monitored medication

trial by pediatricians with expertise in the area; and 2) information about their child's

response to the medication, allowing for a more informed decision about continuing or discontinuing treatment. This medication trial is reported in Chapter 4 of this dissertation.

Screening Measures

Telephone screening questionnaire. Potential participants were asked questions based on inclusion and exclusion criteria in order to confirm whether children were eligible to participate in the study.

Demographic questionnaire. This questionnaire, modelled after the National Household Survey (Statistics Canada, 2011), asked parents general questions about family variables such as marital status, family income, and ethnicity. The information was used to describe the participant sample. This questionnaire was completed during the screening stage of the study.

Child Behaviour Checklist (CBCL; Achenbach & Rescorla, 2001). The CBCL, a parent-report questionnaire, is one of the most widely used instruments to evaluate behavioural and emotional problems in children and is used to screen children for mental health problems. Previous research findings provide strong evidence for the reliability, as well as the convergent and discriminative validity, of the CBCL (Nakamura, et al., 2009). In this study, parents completed the CBCL at screening and any child who received a t-score of 70 or greater on any of the DSM – oriented scales was excluded from participating in the TD group.

Conners' Parent & Teacher Rating Scale-Third Edition- (Parent: CPRS-3 & Teacher: CTRS-3; Conners, 2008). The CPRS-3 and CTRS-3 are 110-item and 115-item behaviour rating scales used to evaluate problem behaviours in the home and school settings in children aged 6 to 18 years. These measures are the most widely used

measures of ADHD symptoms in treatment trials. The CPRS-3 and CTRS-3 forms have excellent internal reliability (Conners, 2008). High scores on these measures indicate high symptom levels. In this study, both parent and teacher forms were used at screening to verify that children in the TD group did not have clinically elevated symptom levels (i.e., t-score of 70 or greater) and to confirm ADHD status.

Sleep Evaluation Questionnaire (SEQ; Mindell & Owens, 2003). The SEQ is a parent-report sleep-screening instrument that is used to obtain information on children's current and past sleep habits and problems, medical history, and family demographics. In this study, this screening measure was used to obtain general information about children's habitual sleep patterns (e.g., bedtime, wake time, sleep habits), and to confirm that the child did not meet any exclusion criteria with respect to sleep (e.g., evidence of sleep disordered breathing, restless legs syndrome).

Pubertal Developmental Scales (NICHD Study of Early Child Care and Youth Development, 2000). The *Girls' & Boys' Pubertal Developmental Scales* are composed of 5 items and used to assess Tanner stage. Both measures are widely used, and have excellent reliability and validity (Marshall & Tanner, 1969, 1970). In this study, these questionnaires were completed by the child's parent. Any child who received a score indicating that he/she was above Tanner stage 2 was excluded from the study.

Outcome Measures

Groups were matched on age and sex at an individual participant level. In all analyses, raw scores were used when possible as the constructs that were measured are generally stable over time (Spencer, Bornholt, & Ouvrier, 2003).

Sleep.

Objective measures of sleep and sleepiness.

Actigraphy. (Ambulatory Monitoring Inc). Actigraphy involves measurement of motor activity using an accelerometer-based device. Actigraphs resemble a small wristwatch and are worn on the non-dominant wrist. Previous studies have shown that actigraph data provide valid and reliable estimates of when participants are asleep and awake, as well as a means of assessing sleep quantity variables such as sleep latency and duration (Sadeh, 2011). Actigraphy has been found to have good face validity and reliability (Sadeh, 2011). In this study, the variables of interest for data analysis included sleep duration (i.e., TIB), total minutes spent asleep (i.e., TST), sleep onset latency (SOL; i.e., how long it took to fall asleep after lights out), sleep efficiency (SE; i.e., amount of time asleep divided by amount of time in bed), wake after sleep onset (WASO; i.e., minutes of wakefulness after sleep was initiated), bedtimes, and wake times. Parents completed sleep diaries which consisted of questions assessing various sleep-related parameters (i.e., lights out time, sleep onset time, number of night awakenings, and wake time). This information was used to set the *down* interval which was used in data analysis

Multiple Sleep Latency Tests (MSLT). The MSLT protocol involved four nap opportunities (10:00, 12:00, 14:00, 16:00) during each testing day. For each nap opportunity, the child was told to lie down on a bed with his/her eyes closed and that he/she should not resist sleep. Each nap opportunity was terminated after 20 min if the child did not fall asleep. If the child fell asleep, he/she was awoken after 15 min from the time of sleep onset. The variables of interest for this study were the mean number of naps that included sleep (range: 0-4), and the mean SOL during each day's naps (range: 0-20 min). Both of these variables are indicators of sleepiness.

Subjective measures of sleep and sleepiness.

Children's Sleep Habits Questionnaire (CSHQ; Owens, Spirito, & McGuinn, 2000). The CSHQ is a 45-item parent-report sleep-screening instrument designed for use with school-aged children. Higher scores indicate more sleep problems. Previous research has documented the measure's strong psychometric properties (Owens et al., 2000). Parents rate children's sleep behaviours on a 3-point scale of frequency (usually = 5-7 times/week, sometimes = 2-4 times/week, rarely = 0-1 time/week). The variables of interest for the current study were raw scores for the sleep duration subscale and the sleep onset latency subscale.

Modified Epworth Sleepiness Scale- Child Version (MESS; Melendres et al., 2004). This scale consists of eight items that represent different situations in which a child may fall asleep (e.g., reading a book, driving in a car). This measure is approaching well-established for evidence-based assessment and has strong reliability (Lewandowski, Toliver-Sokol, & Palermo, 2011). Higher scores on the measure represent more sleepiness. In this study, each item was rated by parents on a 4-point scale (ranging from 0 = no chance of dozing to 3 = high chance of dozing). A total raw score was calculated (range: 0-24), and was the variable of interest for data analysis.

ADHD Rating Scale-IV Modified – Testing Observations – RA Report ((RAR; 2009). This 22-item questionnaire asks a series of questions about participant behaviour. Only one question was used for the analyses. RAs were asked to circle the number that best describes the child's sleepiness during the testing session on a scale from 1 (alert) to 5 (tired). The variable of interest for data analysis was the total raw score for the sleepiness item (range: 1-5).

Child Sleep Self-Report (CSSR; Owens et al., 2000). The CSSR is an 18-item self-report of sleep behaviours and habits (e.g., go to bed at the same time every night, sleep too little, take naps during the day). The CSSR is correlated with the CSHQ, and has strong reliability (Lewandowski et al., 2011). The CSSR uses the same 3-point rating scale as the CSHQ (i.e., usually = 5-7 times/week, sometimes = 2-4 times/week, rarely = 0-1 time/week). Higher scores represented greater sleep problems. The variable of interest for data analysis was the total raw score.

Child's Pictorial Sleepiness Scale (CPSS; Maldonado, Bentley, & Mitchell, 2004). This scale displays five cartoon faces representing degrees of sleepiness. In this measure, children are asked to indicate their sleepiness by circling the face that best matches how they feel at a particular time. The anchors for this measure are 1 (very alert face) to 5 (very sleepy face). This measure has good validity and is particularly useful with children (Maldonado et al., 2004). The CPSS was administered four times throughout each testing session (i.e., once prior to each of the four naps). The variable used in analyses was the average sleepiness score across the four ratings.

Attention.

Objective measures of attention.

Conners' Continuous Performance Test – Second Edition (CPT-II; Conners, 2000). The Conner's Continuous Performance Test-II (CPT-II) is a 14 min, computer-administered test that measures aspects of attention (i.e., inattention, sustained attention, vigilance). Visual stimuli (single letters) are randomly presented on a computer screen at three different rates: once per second (s), once every 2 s, or once every 4 s, for a total of 360 trials. The participant is asked to press a button in response to every stimulus except

the indicated target signal (the letter X). The CPT-II has high split-half reliability for omission and commission error scores, and high test–retest reliability for individuals with ADHD (Campbell, Brown, Cavanaugh, Vess, & Segall, 2008). Typically, commission errors represent impulsivity while omission errors represent inattention. However, commission errors may also reflect slow responses to preceding targets (Conners, 2000). Variables from the CPT-II used in this study included the total number of omissions (missed targets), total number of commissions (false hits), and hit RT. These three variables were of interest as they were expected to be most impacted by sleep restriction, and are commonly used in the literature.

Children's Colour Trails Test (CCTT; Williams et al., 1995). The CCTT is a two-part paper-and-pencil task. The first part of the task (CCTT-1) has children connect dots numbered 1 through 15 and assesses perceptual tracking. In the CCTT-2, children are presented with an array of numbered dots, 15 yellow dots and 15 pink dots. The task requires children to connect dots numbered 1 through 15, alternating between pink and yellow. This task assesses divided attention and sequencing in addition to perceptual tracking, sustained attention, and graphomotor skills. The CCTT has been shown to have good test-retest reliability and good validity (Llorente, Voigt, Williams, Frailey, Satz, & D'Elia, 2009). Given that the CCTT-1 is primarily a perceptual tracking task, this was not used in the analysis, rather the variable of interest for the current study was the time in seconds for task completion of the CCTT-2.

Subjective measures of attention.

Conners' Parent & Teacher Rating Scale-Third Edition (Conners 3-P & Conners 3-T; Conners, 2008). The CPRS-3 and CTRS-3 (described above) were used to assess

subjective parent and teacher reports of children's inattention. The variable of interest

was the raw score from the DSM-IV Predominantly Inattentive subscale for both parents

and teachers (range: 0-30).

ADHD Rating Scale-IV Modified – Testing Observations – RA Report (RAR;

2009). RAs used the RAR (described above) to rate symptoms of inattention ($n = 9$) and

symptoms of hyperactivity ($n = 9$) items by circling the number that best described the

child's behaviour during the testing session on a scale from 0 (never or rarely) to 3 (very

often), with an option to circle Not Applicable. For the attention subscale, the RA rating

of the child's inattention during the testing session was the total number of scores of

either 2 or 3 on the inattention subscale (range: 0-9).

Self-Report of Symptoms (Child) – Child Self-Report (ADHD-CSR; 2009). The

ADHD-CSR is a 33-item questionnaire that asks children to rate how frequently during

the last week they engaged in each of the listed behaviours on a 3-point scale ranging

from 0 (never) to 2 (usually). Questions on this measure address behaviours pertaining to

attention, hyperactivity, oppositional behaviour, anxiety, and depression. In this study,

the variable of interest was the total raw score on the inattention subscale (range: 0-18).

Emotion.

Objective measures of emotion.

Affective Response Task (ART; Leotta et al., 1997). The ART is a task assessing

emotion that has been found to be sensitive to sleep restriction in children and

adolescents. This task was composed of a set of 15 visual stimuli from the International

Affective Picture System (IAPS; Lang et al., 2005) and contained various pictures

depicting images such as pollution, puppies, and roller coasters, which were intended to

elicit emotional reactions. Following each picture, children are asked to report their response to the image on a scale measuring 0-158 mm for each of six different emotions; happy, sad, scared, angry, disgusted, interested. In this study, the two scores used in data analysis were the mean positive affective response score (i.e., happy, interested) and the mean negative affective response score (i.e., sad, scared, angry, disgusted).

Subjective measures of emotion.

Emotion Regulation Checklist-Revised (ERC-R; Shields & Cicchetti, 1997). The ERC-R is a paper/pencil questionnaire that consists of 24 items that assesses parents' or teachers' perceptions of their child's typical methods of managing emotional experiences. Each item is rated on a 4-point scale of 1 (rarely/never) to 4 (almost always). The ERC contains questions pertaining to emotional lability, dysregulated negative affect, appropriate emotional expression, empathy, and emotional self-awareness. There are two main subscales that are calculated from the ERC-R, the Lability/Negativity subscale and the Emotion Regulation subscale. The total scores have good internal consistencies, assessed by Cronbach's alpha (Shields & Cicchetti, 1997). The scores used in this study were the parent and teacher ratings of Emotion Regulation (raw score; range: 8-32), where high scores indicate good emotion regulation, and Lability/Negativity (raw score; range: 15-45), where high scores indicate greater emotional lability/negativity.

ADHD Rating Scale-IV Modified – Testing Observations – RA Report (RAR; 2009). RAs used the RAR (described above) to rate emotional functioning by circling the number that best described the child's mood during the testing session on a scale from 1 (happy) to 5 (sad). The variable of interest for data analysis was the raw score for this item (range: 1-5).

Children's Emotion Management Scales (CEMS; Zeman, Shipman, & Penza-Clyve, 2001). The CEMS is a self-report questionnaire examining children's sadness (11 items), worry (10 items), and anger (12 items). Using a Likert scale of 1 (hardly ever), 2 (sometimes), or 3 (often), children respond to items that comprise three subscales including Inhibition (suppression of emotional expression), Dysregulated Expression (inappropriate outward expression of emotions) and Emotion Regulation Coping (children's adaptive methods of emotion management). The variables of interest for the current study were the total raw score for the Dysregulated Expression subscale (range: 9-27), where higher scores indicate more dysregulation, and the total raw score for the Coping subscale (range: 12-36), where higher scores indicate better coping.

Cognitive functioning.

Objective measures of cognitive functioning.

Short-term memory. Short-term memory (STM) was assessed using a verbal digit span task (range: 0-16) and a visual sequencing task (range: 0-23). Participants were asked to repeat sequences of numbers (digit span), and point out visual patterns (visual sequencing task). Performance was based on the child's ability to repeat the sequences and patterns in the same order as presented by the administrator. Higher scores indicated better performance. A composite of the two raw scores was calculated for short-term memory and used in data analysis.

Working memory. Working memory (WM) was assessed using a similar verbal digit span task (range: 0-14) and visual sequencing task (range: 0-23). Participants were asked to repeat the digits they heard in reverse order, and point out patterns of visual sequences in reverse order from how they were presented. Higher scores indicated better

performance. A composite raw score was calculated from the two raw scores and was used as the WM score for data analysis in the current study.

Subjective measures of cognitive functioning.

Conners' Parent & Teacher Rating Scale-Third Edition (Conners 3-P & Conners 3-T; Conners, 2008). Raw scores from the CPRS-3 (range: 0-30), and CTRS-3 (range: 0-18) Learning Problems subscales were used in the analysis of cognitive functioning.

Statistical Considerations

Repeated measures multivariate analysis of variance (RM-MANOVA) were used to examine the effect of experimental sleep manipulation on outcome variables including sleep, attention, emotion, and cognitive functioning. The primary outcomes of interest were a main effect of condition and the sleep condition by group interaction. The main effect of group is reported separately at the beginning of each section. Subjective and objective measures were examined in separate RM-MANOVA analyses. Wilks' lambda was used as the output of MANOVA, and an alpha level of .05 was used to determine statistical significance. Partial eta squared (η^2) values were used for effect sizes, and were interpreted using Cohen's 1969 approximate benchmarks whereby .01 was a small effect size, .06 was medium, and .14 was large (Richardson, 2011). Exploratory analyses were conducted and are presented at the end of the results section.

A power analysis was conducted a priori using effect sizes from objective measures of attention in a previous similar study, where $\eta^2 = 0.32$ for direct measures of attention (Gruber et al., 2011). Based on this effect size, using the online calculator G*Power (Faul et al., 2007), with estimated power at 80%, and an alpha of 0.05, the required resulting total sample size was 26 participants.

Data for participants who did not complete all phases of the study were excluded; however, there were some missing data points throughout individual measures (percentage of missing data ranged from 0-14%). Little's MCAR test (Little, 1988) was used to determine that the data were missing at random for each outcome measure and expectation-maximization methods were used to generate missing values in SPSS.

Prior to analyses, statistical assumptions were checked. Outliers were present in some outcome variables, and some data were not normally distributed. Therefore, data were transformed by taking the square root of the variables if moderately skewed, or by applying a logarithmic transformation if strongly skewed. Results were not significantly affected whether transformed data or raw data were used. Thus, the final analyses included data from all participants and variables were not transformed.

Results

To determine whether the sleep manipulation was successful, data were examined to ensure criteria for minimum sleep restriction were met. As per previous literature, participants had to achieve a minimum mean restriction of 30 min less TIB per night for each of the studied nights (Vriend et al., 2013) for entry into the remaining analyses. Of the 52 participants who completed the entire sleep manipulation protocol, 12 (5 ADHD; 7 TD) did not meet minimum entry criteria and were not considered to have followed the sleep restriction protocol. Therefore, there were 40 participants in total (18 ADHD; 22 TD) who completed the entire protocol and met minimum criteria. In order to match the groups for sample size and sex ratio, four additional TD participants were excluded. These four participants were selected based on missing critical actigraph data points. Therefore, data from 36 participants, with 18 participants in each group, were included in

the data analyses. Half of the participants in each group completed the Typical condition first, and the other half completed the Restricted condition first. A RM-MANOVA was conducted for each outcome measure with order as the between-subjects variable and there were no significant main effects of order. Given that teachers and RAs were blind to experimental condition, data from teachers and RAs were preliminarily analyzed separately from parent reports and child self reports to determine if blinding influenced results. No differences in results were found, therefore, all subjective ratings were analyzed and reported together to reduce the number of analyses.

Sample Characteristics

There were 18 participants (14 male; 4 female) in each group. Participants ranged from 6 to 11 years of age. The mean age was 8.28 years ($SD = 1.45$) in the TD group and 8.56 years ($SD = 1.58$) in the ADHD group. Groups did not differ significantly in age (F $(1, 34) = 0.30, p = .59, \eta^2 = .01$).

Data on parental education, family income, ethnicity, and family composition were obtained and groups were not significantly different on any of the variables assessed. See Table 3.1 for all descriptive statistics for sample characteristics.

Participants had to have an estimated full-scale intelligence quotient (FSIQ) ≥ 80 to be included in data analysis. The mean estimated FSIQ for the ADHD group was 99.92 ($SD = 10.86$), and the mean estimated FSIQ for the TD group was 107.98 ($SD = 9.50$). These means were significantly different ($t (34) = -2.37, p = .02$), however both groups were in the Average range (range: 83-124). Half of the children in the ADHD group either had a comorbid learning disability ($n = 5$) or were at risk for a learning disability (n

= 4). None of the children in the TD group had mental health disorders or learning

disabilities.

Sleep Characteristics at Baseline

     Group differences in sleep parameters.

     Objective measures. Results from the overall MANOVA examining TIB, TST,

SOL, SE, bedtime and wake time revealed that there were no significant differences

between groups on these variables (Wilks' lambda = 0.81, F (6, 29) = 1.12, p = .37, η^2 =

.19). Children in both groups were spending on average ~10 h TIB during the baseline

period, and just over 8 h TST. Both groups had an SOL of approximately 30 min, and SE

was ~86% for both groups. Bedtimes and wake times were also similar. Means were not

significantly different for any of the objectively measured sleep variables between groups

(see Table 3.2).

     Subjective measures. A MANOVA was conducted including parent rated sleep

duration and sleep onset delay, and child rated sleep. Results showed that overall children

did not significantly differ on parent and child rated sleep variables at baseline (Wilks'

lambda = 0.92, F (3, 32) = 0.90, p = .45, η^2 = .08). See Table 3.2 for means and SD.

Effect of Sleep Manipulation

     The results of tests for group differences are presented first, followed by tests for

main effects of sleep condition and interaction effects. For effects of sleep manipulation

on sleep, two RM-MANOVAs were conducted, one examining objective outcome

variables for sleep (i.e., actigraphy data for TIB, TST, SOL, SE, WASO, bedtime, and

wake time), and one for subjective outcome variables (i.e., parent-rated sleep duration

and SOL). Two RM-MANOVAs were conducted for sleepiness measures, one for

objective measures (i.e., number of nap opportunities that included sleep and nap onset latency), and one for subjective measures (i.e., parent, RA, and child rated sleepiness). Two RM-MANOVAs were conducted for each domain of daytime functioning (i.e., attention, emotion, cognitive functioning), one for objective measures and one for subjective measures. Objective outcome variables for attention included CPT-II data for omissions, commissions, hit RT, and the CCTT-2 completion score. Subjective outcome variables for sleep were parent, teacher, RA, and child rated inattention. Objective outcome variables for emotion were the ART-positive and ART-negative scores and subjective measures were parent and teacher rated emotion regulation and lability/negativity, RA rated mood, and child rated emotional dysregulation and coping. Objective measures of cognitive functioning were performance scores for STM and WM tasks. Subjective outcome variables were parent and teacher rated learning problems.

Between-Group Differences Related to Sleep and Daytime Functioning

  Sleep and sleepiness.

  Objective measures. RM-MANOVA showed that there was no significant main effect of group on sleep variables as measured by actigraphy (Wilks' lambda = 0.74, F (7, 28) = 1.41, p = .24, η^2 = .26). There was no significant main effect of group on objective measures of sleepiness as measured by MSLT (Wilks' lambda = 0.95, F (2, 33) = 0.93, p = .40, η^2 = .05).

  Subjective measures. There was no significant main effect of group on subjectively reported sleep (Wilks' lambda = 0.93, F (3, 32) = 0.83, p = .49, η^2 = .07), and no significant main effect of group on subjectively reported sleepiness (Wilks' lambda = 0.94, F (3, 32) = 0.57, p = .64, η^2 = .05).

Daytime functioning (attention, emotion, cognitive functioning).

Objective measures. There were no significant main effects of group on objective measures of attention (Wilks' lambda = 0.92, F (4, 31) = 0.69, p = .60, η^2 = .08), emotion (Wilks' lambda = 0.95, F (2, 33) = 0.90, p = .42, η^2 = .05), or cognitive functioning (Wilks' lambda = 0.87, F (2, 33) = 2.41, p = .11, η^2 = .13).

Subjective measures. There were significant main effects of group on subjective measures of attention (Wilks' lambda = 0.25, F (4, 31) = 23.04, p = .00, η^2 = .75), emotion (Wilks' lambda = 0.52, F (7, 28) = 3.71, p = .01, η^2 = .48), and cognitive functioning (Wilks' lambda = 0.50, F (2, 33) = 16.60, p = .00, η^2 = .50), whereby children with ADHD were rated as having more problems compared to the TD group by both parents and teachers. RAs (blind to diagnostic group) and the children themselves did not report any significant group differences on subjective ratings of daytime functioning.

Differences in Sleep and Daytime Functioning Between Sleep Conditions and Interaction Effects Between Group and Sleep Condition

Sleep and sleepiness.

Objective measures. Results from RM-MANOVA revealed that there was a significant main effect of sleep condition on sleep variables as measured by actigraphy (Wilks' lambda = 0.06, F (7, 28) = 69.21, p = .00, η^2 = .95). There was no significant interaction between group and sleep condition (Wilks' lambda = 0.96, F (7, 28) = 0.19, p = .99, η^2 = .05). Results from the univariate tests for sleep condition showed that children had on average significantly less TIB, less TST, faster SOL, and decreased WASO, but no change in SE during Restricted condition compared to Typical condition. Bedtime was

significantly later in Restricted condition compared to Typical condition and wake times were not significantly different. See Table 3.3 for all means, SD, and ANOVA results for sleep variables as measured by actigraphy.

A RM-MANOVA was conducted to examine whether there were any effects of condition on objective measures of sleepiness (See Table 3.4 for means and SD). Results showed that there was no significant main effect of condition (Wilks' lambda = 0.94, F (2, 33) = 1.04, p = .36, η^2 = .06), and no significant interaction (Wilks' lambda = 0.88, F (2, 33) = 2.35, p = .11, η^2 = .13).

Subjective measures. RM-MANOVA showed that for subjectively measured sleep (i.e., parent rated sleep duration and sleep onset latency) there was no significant main effect of sleep condition (Wilks' lambda = 0.80, F (3, 32) = 2.76, p = .06, η^2 = .21), and no significant interaction between group and sleep condition (Wilks' lambda = 0.90, F (3, 32) = 1.24, p = .31, η^2 = .10). See Table 3.5 for means and SD.

Results from the RM-MANOVA showed that for subjectively measured sleepiness (see Table 3.4 for means and SD), there was no significant main effect of condition (Wilks' lambda = 0.85, F (3, 32) = 1.83, p = .16, η^2 = .15, and no significant interaction (Wilks' lambda = 0.93, F (3, 32) = 0.84, p = .48, η^2 = .07).

Effects of sleep manipulation on daytime functioning.

Attention.

Objective measures. A RM-MANOVA was completed (see Table 3.6 for means and SD) and revealed that there was a main effect of condition (Wilks' lambda = 0.74, F (4, 31) = 2.70, p = .05, η^2 = .26), indicating that collapsed across group, there was a significant difference in attention between Restricted and Typical sleep weeks. The

interaction between condition and group was not significant (Wilks' lambda = 0.77, F (4,

31) = 2.39, p = .07, η^2 = .24). Examination of the univariate tests (see Table 3.6) for sleep

condition revealed that omissions were significantly higher and commissions were

significantly lower during Restricted condition compared to Typical condition. There

were no significant differences between sleep conditions for hit RT and CCTT-2

performance.

Subjective measures. Parent, teacher, RA, and child rated inattention were

analyzed using RM-MANOVA (see Table 3.7 for means and SD). Results revealed that

there was no significant effect of condition (Wilks' lambda = 0.86, F (4, 31) = 1.27, p =

.30, η^2 = .14), and no significant interaction between group and condition (Wilks' lambda

= 0.95, F (4, 31) = 0.41, p = .80, η^2 = .05).

Emotional Functioning.

Objective measures. Results from the RM-MANOVA examining children's

performance on the ART (see Table 3.8 for means and SD) revealed that there was no

significant main effect of condition (Wilks' lambda = 0.99, F (2, 33) = 0.09, p = .92, η^2 =

.01), and no significant interaction between group and condition (Wilks' lambda = 0.98,

F (2, 33) = 0.38, p = .69, η^2 = .02).

Subjective measures. Results from the omnibus RM-MANOVA examining

emotional functioning revealed that there was a significant main effect of condition

(Wilks' lambda = 0.63, F (7, 28) = 2.33, p = .05, η^2 = .37). There was no significant

interaction between sleep condition and group (Wilks' lambda = 0.85, F (7, 28) = 0.71, p

= .67, η^2 = .15). Examination of the univariate ANOVAs for condition showed that only

parent ratings of lability/negativity were significantly different, indicating that children

were more emotionally labile and negative during Restricted condition compared to Typical condition (see Table 3.9).

Cognitive Functioning.

Objective measures. A RM-MANOVA was conducted to examine the impact of sleep condition on measures of memory (i.e., short-term memory and working memory). Results showed that there was no significant main effect of condition (Wilks' lambda = 0.99, F (2, 33) = 0.16, p = .85, η^2 = .01). There was also no significant interaction between condition and group (Wilks' lambda = 0.99, F (2, 33) = 0.18, p = .84, η^2 = .01). See Table 3.10 for means and SD.

Subjective measures. The multivariate test examining subjective measures of parent rated cognitive functioning and learning (see Table 3.10 for means and SD) revealed that there was no main effect of condition (Wilks' lambda = 0.90, F (2, 33) = 1.84, p = .18, η^2 = .10), and no significant interaction between group and condition (Wilks' lambda = 0.95, F (2, 33) = 0.97, p = .39, η^2 = .06).

Secondary Data Analyses

1) Analyses of participants with mean nightly TST restriction greater than or equal to 30 min. The criteria for inclusion into data analysis was average TIB restriction of at least 30 min per night. However, TIB does not equal TST and therefore does not indicate how much time was spent sleeping. Given that the participants in this sample were on average only mildly sleep restricted, a secondary, exploratory analysis was conducted on data from children who were able to restrict TST by at least 30 min per night (n = 19; 9 ADHD, 10 TD). Results showed that this subgroup of children reduced their average TST by ~ 67 min.

There was no significant main effect of group on sleep variables, using either subjective or objective measures. Groups were significantly different on objectively measured sleepiness (Wilks' lambda = 0.58, F (2, 16) = 5.84, p = .01, η^2 = .42), where the ADHD group slept during more nap opportunities and had shorter SOLs during naps, but did not differ on subjectively measured sleepiness. With respect to daytime functioning, the ADHD and TD groups were significantly different on subjective measures of attention (Wilks' lambda = 0.24, F (4, 14) = 11.06, p = .00, η^2 = .76), objective measures of emotion (Wilks' lambda = 0.68, F (2, 16) = 3.69, p = .05, η^2 = .32), and subjective measures of cognitive functioning (Wilks' lambda = 0.49, F (2, 16) = 8.47, p = .003, η^2 = .51).

As in the larger analysis, there was a significant main effect of sleep condition on objectively measured sleep (Wilks' lambda = 0.03, F (7, 11) = 61.40, p = .00, η^2 = .98). Examination of univariate analysis revealed that TIB, TST, SE, and bedtime were all significantly different between sleep conditions. There were no significant differences in SOL, WASO, and wake times between conditions (see Table 3.11). There were no significant main effects of sleep condition on subjectively rated sleep, or subjectively and objectively rated sleepiness. There were no significant interactions between sleep condition and group on any sleep variables.

Results showed that there were no significant main effects of sleep condition, and no significant sleep condition by group interactions on any attention, emotion, or cognitive functioning variables.

2) Analyses of participants recoded into restricted group or no change group.
Using the methods described in Sadeh et al. (2003), the participants who were able to

follow the TIB reduction protocol ($N = 36$) were categorized into two groups based on how effectively they were able to restrict their sleep. Participants who restricted their TST by an average of 30 min or greater in the Restricted condition compared to Typical condition were defined as the Sleep Restricted group ($n = 16$), and children who restricted their sleep less than an average of 30 min were defined as having no change in sleep ($n = 16$). Results from MANOVAs with difference scores on daytime functioning outcome measures revealed that there was no difference in performance on any daytime functioning measures between the Sleep Restricted group and the group that demonstrated no change in sleep duration.

Discussion

Effectiveness of the Sleep Manipulation

Results showed that most participants were able to adhere to the sleep manipulation protocol. Based on previous research (Sadeh et al., 2003; Vriend et al., 2013), a minimum 30 min reduction in TIB was used as inclusion criterion for data analysis. Using this criterion, results showed that children with ADHD successfully reduced their TIB by ~53 min and TD children reduced their TIB by ~56 min during Restricted condition compared to Typical condition. Examination of bedtimes revealed that both groups followed the manipulation protocol, and successfully moved bedtime close to 1 h later (53 min in the ADHD group, 49 min in the TD group). Wake times were consistent for both groups and across both sleep conditions. While TIB was successfully reduced, the results for TST showed that children with ADHD were sleeping on average only ~16 min less, and TD children ~25 min less during Restricted condition compared to Typical condition. This discrepancy between TIB and TST was due to the fact that

children in both groups fell asleep ~10-11 min faster in the Restricted condition, as a result of increased sleep pressure. Furthermore, examination of the WASO data revealed that during Restricted condition, the TD group reduced their WASO by ~20 min, and the ADHD group reduced their WASO by ~9 min. Therefore, while TIB was restricted, the effect on TST was minimized given that children had faster SOL and less WASO.

The results of this study also showed that while TIB and TST were significantly different between Restricted and Typical conditions (i.e., 55 min less TIB, 21 min less TST), the difference did not lead to more daytime sleepiness. Children were not rated as sleepier, nor did MSLT data indicate that they were sleepier during the Restricted condition compared to the Typical condition.

Impact of Sleep Manipulation on Daytime Functioning

Children with ADHD were subjectively rated as having more difficulty with attention, emotions, and cognitive functioning compared to their TD peers, but there were no significant differences between groups in performance on objective tasks. Negative consequences of mild sleep restriction were found for objective attention tasks, and for subjectively rated emotion, regardless of group. The ADHD group did not appear to have more difficulty with daytime outcomes following Restricted condition compared to their TD peers.

Despite a very mild TST restriction of ~20 min, some objective measures of attention (i.e., omission and commission errors of the CPT-II) were significantly different when sleep was restricted. This finding is consistent with previous research (Gruber et al., 2011). Hit RT and completion time for the CCTT-2 task were not significantly different, which was inconsistent with previous findings (Gruber et al., 2011; Vriend et al., 2013).

Results showed that CPT hit RT (i.e., the average speed of response for correct responses) did not change between sleep conditions. On the CCTT-2 task, overall task completion time was also not significantly affected by sleep restriction, indicating that the mild sleep restriction did not impair children's ability to complete a short task requiring attention to sequencing.

Hit RT from the CPT reflects response time for correct responses only. Omission and commission errors provide more insight into task vigilance. Results showed that omission errors were higher during Restricted condition, suggesting that participants were either too slow to respond, or did not respond to target stimuli at all. Participants also demonstrated decreased commission errors (i.e., fewer responses to non-target) during the Restricted condition. Previous research has suggested a relationship between sleep and processing speed (Buckhalt, El-Sheikh, & Keller, 2007), as such, considering both omission and commission errors together, a mild reduction in sleep may have impacted the speed at which children accurately processed and differentiated a target from a non-target resulting in more omission and fewer commission errors. Mild sleep restriction may have made it more difficult for children to sustain their attention for long repetitious tasks, as compared to a much shorter task such as the CCTT-2. Sadeh et al. (2003) examined the CPT and found that hit RT was significantly improved following sleep extension, while none of the CPT variables were significantly different following sleep restriction. Similarly, Vriend et al. (2013) used the CCTT-2 task and found that task completion time was slower following sleep restriction compared to extended sleep.

Results showed that subjective parental ratings of emotional lability/negativity were significantly different between Restricted and Typical conditions. Changes in

emotional lability/negativity may have been the most obvious to parents (i.e., child was grumpier), as these items represented behaviours typical of what parents observe on any given day that a child experienced less sleep than normal. Furthermore, parents had the opportunity to observe their children at times when they may have been feeling naturally tired (i.e., at their regular bedtime when on sleep restriction schedule). Previous research with respect to teacher ratings is inconsistent. Similar to the null results in the current study, Fallone et al. (2005) did not find significant differences in teacher ratings of children's emotions (i.e., sad affect, emotional lability). On the other hand, Gruber et al. (2012) found that teachers rated children as more emotionally labile following sleep restriction compared to baseline, and also that children who extended their sleep showed improved scores on emotional lability compared to baseline. Results for child self-reports of emotional functioning were consistent with those of Vriend et al. (2013) in that no significant differences were noted between conditions. This was the first study to include RA ratings of emotional functioning, and ratings were not significantly different between conditions. The null finding may have been due to the fact that children were able to regulate themselves in the presence of the RA (i.e., somewhat unfamiliar person), and in the structured, novel testing environment (Henderson & Fox, 1998).

Results on the objective measures of emotion showed that no significant changes were found for either positive or negative affect. These findings were unexpected given that a modified version of the task that was used in Vriend et al. (2013), which was found to be sensitive to sleep restriction was also used in the current study. Vriend et al. (2013) found that the children responded to the task with more positive affect during extended sleep compared to restricted sleep, but there were no differences in negative affect

between extended and restricted conditions. One possible for the null finding in this study compared to the significant findings in Vriend et al. (2013) is the absence of the extended sleep condition in this study. A second factor that may have resulted in the null finding is that the ART task was modified in the current study to include 15 pictures instead of 30 pictures. The decision to shorten the task was made to ensure that difficulty with sustaining attention to task did not interfere with task completion and to reduce overall burden of the testing procedures.

No significant changes in performance were found for the objective measures of cognitive functioning. The STM and WM tasks were short tasks that did not require sustained attention for a lengthy period of time. These findings are similar to previous research where objective measures of memory were not significantly affected by sleep restriction (Sadeh et al., 2003). While Vriend et al. (2013) found significant differences between extended sleep and restricted sleep, the difference may have been due to a larger difference in sleep between manipulation weeks.

The results for subjectively rated attention (parent, teacher, RA, and child self-report) were not significantly different between Restricted and Typical conditions in the current study. Previous studies found significantly higher levels of inattention following cumulative sleep restriction compared to extended sleep (Vriend et al., 2013), and following sleep restriction (i.e., 6.5-8 h TIB) compared to optimized sleep (i.e., 10 h TIB) as in Fallone et al. (2005). It is likely that the sleep restriction in the current study was too mild to significantly impact subjective observations. Subjective measures of cognitive functioning (parent and teacher ratings) were also not significantly different between Restricted and Typical conditions.

Overall, the results of this study showed that children were able to reduce their TIB and their TST, however, the impact on daytime functioning was minimized due to a recovery of sleep loss with a shorter SOL and reduced WASO. Despite a very mild reduction of TST (~20 min), some significant changes in daytime functioning were found. The significant findings in the current study were generally consistent with the literature. In general, the specific impact of mild cumulative sleep restriction on daytime functioning in children remains unclear, however there is mounting evidence for changes in sustained attention, and some aspects of emotional functioning. Given that the reduction in TST was minimal in the whole group studied, exploratory analyses were conducted to determine whether the sleep restriction was too mild to detect changes. Exploratory analyses of the subsample of children who restricted their TST by a minimum of 30 min ($n = 19$) showed that there were no significant main effects of condition on any of the measures, and no significant group by condition interactions. The second exploratory analysis suggested that even children who restricted sleep by 30 min or greater in one condition compared to children with no change in sleep, showed no differences in daytime functioning.

Factors that Influence Effectiveness of Sleep Manipulations

Three factors that may have contributed the study findings are: 1) baseline sleep may play an important role in children's response to mild sleep restriction; 2) different comparison sleep conditions may influence the impact of sleep restriction on daytime functioning; and 3) circadian and homeostatic processes may have played a role.

With respect to baseline sleep, it may be that when children who are mildly sleep restricted at baseline are given the opportunity to extend or optimize their sleep, their

daytime performance on objective measures improves. Conversely, it may be that when children are sleep satiated at baseline (like the current sample) and sleeping well, a mild sleep restriction does not significantly impact their daytime functioning in a broad and clinically significant manner. While there is considerable debate on optimal sleep duration in children (Matricciani, Olds, Blunden, Rigney, & Williams, 2012), researchers in the field of experimental sleep restriction have defined optimized sleep (i.e., sleep satiation) as 10-11 h TIB for school-aged children (Biggs et al., 2010; Fallone et al., 2001; Fallone et al., 2005; Randazzo et al., 1998). The results from the current study and those of Gruber et al. (2011) were similar in that participants in both studies had TIB of approximately 10-10.5 h at baseline (both studies were conducted with Canadian children). Participants in both Vriend et al. (2013), who included children aged 8-12 years, and Sadeh et al. (2003), who included children 9-12 years of age, had a total TIB of 8.7-8.8 h at baseline. Sadeh et al. (2003) only showed improvements on one aspect of the CPT following sleep extension. Furthermore, results from the current study showed that when sleep was mildly restricted in otherwise sleep satiated children, the effects of sleep restriction were counteracted by reduced SOL and WASO. Therefore, daytime functioning was either minimally, or not at all impacted.

The type of sleep condition to which outcomes following sleep restriction are compared (i.e., optimized or extended sleep) likely influences the results of experimental sleep manipulation studies. While some of the findings in the current study were consistent with previous research, there were some findings that were not replicated. For example, it was expected that as in Sadeh et al. (2003), hit RT from the CPT would be significantly slower, and like Vriend et al. (2013), performance on the CCTT-2 would be

slower during Restricted condition. Results showed no significant changes on either hit RT or CCTT-2. Furthermore, results on both the objective emotion and objective cognitive tasks differed from Vriend et al. (2013). Both Sadeh et al. (2003) and Vriend et al. (2013) compared outcome measures following sleep restriction to an extended sleep condition. It is possible that Vriend et al. (2013) observed differences due to improved performance when children had extended sleep opportunities, rather than poorer performance following sleep restriction, while the current study did not include a comparison to a sleep extension condition. Similarly, Sadeh et al. (2003) found significant changes in performance following sleep extension, but no significant changes following sleep restriction. These design differences need to be considered when interpreting results collectively, as they may account for some of the inconsistencies in the literature.

An important factor to consider in the interpretation of the results of this study is the influence of underlying processes related to circadian phase and homeostatic sleep pressure. Objective measures were completed in the morning prior to the first nap so that the nap opportunity did not interfere with the overall sleepiness and possibly act as a confounding variable (as some children fell asleep during nap and others did not). The average wake time in this study was approximately 07:00. As a result, the testing session took place on average between 07:30 and 08:30 and finished prior to the MSLT at 10:00. Testing occurred at a time when homeostatic sleep pressure was low, and circadian phase of wakefulness was strong (Wyatt, 2007). Therefore, both the homeostatic process and sleep circadian rhythm were aligned with a strong propensity for wakefulness, and thus children may have had higher levels of alertness. Results from this study may have

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yielded more significant differences had children been tested later in the day when the difference between the homeostatic sleep pressure process and circadian process was greater and the propensity for sleep was stronger. The influence of circadian phase could be explored in future sleep restriction research in TD children, and particularly in children with ADHD who have been hypothesized as having delayed circadian processes.

Group Differences Between Children with ADHD and TD Children

The second hypothesis of this study was that children with ADHD would be more negatively impacted by sleep restriction than their TD peers. This hypothesis was based on research suggesting that children with ADHD have more problems with sleep and daytime functioning, and therefore would be more negatively impacted by even greater sleep restriction. Consistent with a growing body of literature that shows children with ADHD who are medication naïve do not differ from TD children in objectively measured sleep, the baseline data from this study showed no main effect of group on any sleep variables. Results from the current study are consistent with the results of the only other experimental sleep manipulation study that included children with ADHD (Gruber et al., 2011). Results from both studies suggest that a mild experimental sleep restriction does not significantly impact children with ADHD more than TD children, however more research is needed to confirm these findings given the modest sample sizes in both studies and mild sleep restriction in the present study.

Strengths and Limitations

Much of the previous experimental sleep manipulation literature has examined sleep restriction compared to either optimized sleep or extended sleep. These designs do not allow for a clear understanding of whether children performed worse because of sleep

restriction or better because of sleep extension/optimization. No experimental study to date has examined sleep restriction compared to controlled typical sleep. Therefore, a strength of this study was in the design, where Restricted sleep was directly compared to a controlled Typical sleep condition, which was based on children's habitual sleep schedules. This allowed examination of the differences in performance between Restricted and Typical sleep conditions. This research design also allowed participants and families to acclimatize to the sleep lab and study procedures prior to the sleep manipulation.

The study protocol was designed to examine a mild cumulative sleep restriction. Given that TST cannot be controlled, TIB is the variable that was manipulated. Ethical approval was granted for a maximum restriction of 1 h less TIB per night. Therefore, a limitation of the study is that a 1 h decrease in TIB does not equal a 1 h decrease in TST, and the resulting restriction was much less than originally anticipated. This may have lessened the degree to which changes in various outcomes measures were observed. Finally, some children in both groups were not able to adhere to the protocol and their data were not included. Additionally, given the experimental nature of the study with TIB, while some participants were able to adhere to the protocol, they were not able to reach a mean sleep restriction of 30 min per night, and thus were also not included in analyses. These factors, in combination with logistic limitations (i.e., length of the study, resources) resulted in a somewhat modest sample size in each group.

Another strength of the study was that multiple raters were used (i.e., parents, teachers, RAs, children). Furthermore, teachers and RAs were blinded to sleep condition, and RAs were additionally blind to diagnostic group. While these factors were strengths

of the design, they also draw attention to some limitations, where parents were not blind to either sleep condition, which may have influenced their ratings. Additionally, all RAs were trained in a standardized manner, and best efforts were made to match RAs with the same participant during each visit to reduce inter-rater variability. Due to staffing and schedule constraints, this was not always possible and may have impacted the RA ratings between manipulation weeks.

Finally, all daytime testing was completed in a structured 1:1 setting with standardized administration to control for confounding variables as much as possible. While this was a strength of the design in terms of standardizing the testing both across repeated visits and between participants, there is evidence to suggest that objective measures conducted in this kind of setting do not mimic the outside world and how children perform in their natural home and school environments (Davidson, Cherry, & Corkum, 2015; Stanovich, 2009). The structured testing environment may have impacted children's performance on objective measures, and the ability to detect differences following sleep manipulation. Furthermore, as previously discussed, while the decision to test first thing in the morning was made in order to ensure equal alertness for all participants (prior to nap opportunity), results may have been influenced by circadian and homeostatic processes that promote wakefulness in the morning.

Clinical Implications and Future Directions

The implications of the results of this study relate to both clinical practice and pediatric sleep research. Clinically, given the very limited number of studies available on cumulative sleep restriction, caution in over interpreting results must be taken. However, there is some evidence that daytime functioning outcomes are more likely to deteriorate

as a result of sleep restriction, whereas other outcomes are likely to improve as a result of extended sleep. Furthermore, identification of baseline sleep problems should be completed as a routine part of any assessment (i.e., cognitive and mental health) given that mild cumulative sleep restriction may impact daytime functioning, and sleep problems are common in children, both with and without ADHD, and the impact of sleep restriction on children experiencing sleep problems at baseline may be more profound.

From a research standpoint, there are several important implications to consider to build upon the current literature. Generally, baseline sleep in both TD children and children with ADHD should be considered in future research to explore whether there is a true relationship between baseline sleep and the impact of sleep manipulation on daytime functioning. Furthermore, all experimental studies on cumulative sleep restriction in children to date have examined daytime functioning after one week or less of mild sleep restriction. More research is needed to better understand both the impact of sleep on daytime functioning in the short term and the long term, but also the underlying sleep processes that occur when children's sleep is restricted.

The mild cumulative sleep restriction of 1 h relative to habitual sleep duration reflects a restriction length that occurs naturally for many children (i.e., reading one more chapter in a book, getting home from hockey practice late, watching one more TV show before bed). The decision to use this length of TIB reduction was in part due to practical reasons, such that many children already experience this level of sleep restriction on a regular basis, and in part due to ethical concerns. Given that research shows that adequate sleep is needed for optimal school functioning, there may have been ethical concerns raised by the research ethics board and parents had a more severe, chronic sleep

restriction been proposed. Furthermore, sleep duration recommendations for children are not empirically supported (Matricciani et al., 2013). Therefore, the study design of a 1 h reduction TIB relative to children's habitual sleep allows for examination of daytime functioning outcomes without relying on any assumptions of sleep need. Additionally, four of the five previous studies on experimental sleep restriction in children used a 1 h reduction of TIB, therefore the design of the current study was consistent with previous literature where significant differences were found.

Results showed that while most children were successfully able to adhere to a 1 h reduction of TIB, other sleep parameters interfered with the reduction in TST by effectively recovering lost sleep (i.e., shorter SOL and reduced WASO). This recovery reduced the magnitude of the difference in sleep between Restricted and Typical conditions. Therefore, the results of this study are somewhat limited due to the small difference in actual sleep achieved between conditions. However, given the effect of increased sleep pressure as a result of mild cumulative sleep restriction, it would be interesting to explore sleep and daytime functioning in children with ADHD following acute sleep deprivation compared to typical sleep, and cumulative sleep restriction.

Conclusions

The aim of this study was to examine the impact of sleep restriction on daytime functioning in TD children and children with ADHD. This is only the second experimental sleep restriction study of school-aged children to include a sample of children with ADHD. The ADHD group in this study did not appear to be significantly more affected by sleep restriction than their TD counterparts. More experimental research is needed in this population with a more significant sleep restriction, as the one previous

study showed some evidence that performance of children with ADHD moved from the average range to the clinical range following sleep restriction (Gruber et al., 2011).

Participants in this study experienced only mild sleep restriction, and yet significant differences on an objective attention task and parent-rated emotions were observed. Sleep data showed that children counteracted some of the effects of the sleep restriction by reducing SOL and WASO; however, it is unknown whether this would continue in the long term. It is possible that mild sleep restriction in the long term may elicit more profound impacts on daytime functioning. More research in children with ADHD is needed to confirm these findings, given that such a small sleep restriction in TIB led to changes in sleep (reduced SOL and WASO), as well as impairments in daytime functioning.

Table 3. 1

Descriptive Statistics of Family Variables by Group

	ADHD	TD	χ^2	*p*
Ethnicity (*n* = 32)	15/16 Caucasian; 1/16 multi-racial	15/16 Caucasian; 1/16 multi-racial	0.00	1.00
Parental composition (*n* = 34)	13/17 two-parent; 4/17 single parent	16/17 two-parent; 1/17 single parent	2.11	.15
Maternal Education (*n* = 35)	6	4.50	4.70	.45
Paternal Education (*n* = 29)	2.50	4.00	6.48	.26
Annual family income	5	6	4.86	.43

	ADHD	TD	*t*	*p*
Estimated FSIQ	99.92 (*SD* = 10.86)	107.98 (*SD* = 9.50)	2.37	.02

Note: Median for parental education range: 1 = some high school, 2 = completed high school, 3 = some community college, 4 = completed community college, 5 = some university, 6 = completed university; Annual family income: 1 = < 20, 000, 2 = 20, 001-30 000, 3 = 30 001-40 000, 4 = 40 001-50 000, 5 = 50 001-60 000, 6 = 60 001-70 000, 7 = ≥ 70 001.

Table 3. 2

Descriptive Statistics and Results from the Univariate ANOVAs for Objective and

Subjective Sleep Variables at Baseline

	Mean (*SD*)		ANOVA		
	ADHD	TD	*F*	*p*	η^2
Objective Measures					
Mean TIB	608.57 (35.18)	611.92 (32.11)	0.09	.77	.003
Mean TST	491.05 (57.87)	496.69 (42.57)	0.11	.74	.003
Mean SOL	34.14 (19.12)	29.54 (20.90)	0.47	.50	.01
Mean SE	86.01 (7.38)	86.57 (8.43)	0.04	.84	.001
Mean Bedtime	20:45 (0:39)	20:36 (0:38)	0.45	.51	.01
Mean Wake time	06:53 (0:33)	06:47 (0:21)	0.35	.56	.01
Subjective Measures					
Parent rated sleep duration (CSHQ)	4.66 (1.45)	4.89 (1.71)	0.19	.66	.01
Parent rated SOL (CSHQ)	1.35 (0.68)	1.22 (0.43)	0.45	.51	.01
Child rated sleep (CSSR)	43.39 (3.81)	41.39 (4.18)	2.26	.14	.06

Note: SD = standard deviations; TD = typically developing; TIB = time in bed; TST = total sleep time; SOL = sleep onset latency; SE = sleep efficiency; CSHQ = Children's Sleep Habits Questionnaire (range for sleep duration: 3-9, range for SOL: 1-3); CSSR = Child Sleep Self-Report (range: 0-54).

Table 3. 3

Means and SD of Actigraphy Sleep Variables During Sleep Manipulation by Group and

Results of the Univariate ANOVAs for Sleep Condition

	Mean (*SD*)		ANOVA		
	ADHD (*n* = 18)	TD (*n* = 18)	F	*p*	η^2
Mean TIB Typ	599.35 (30.88)	603.89 (35.73)	317.21	.00	.90
Mean TIB Res	546.30 (24.64)	547.37 (38.09)			
Mean TST Typ	479.94 (60.27)	484.70 (56.13)	4.82	.04	.12
Mean TST Res	463.60 (41.10)	459.19 (60.02)			
Mean SOL Typ	29.69 (15.29)	32.74 (16.67)	18.83	.00	.36
Mean SOL Res	18.99 (7.54)	22.89 (18.05)			
Mean SE Typ	85.15 (9.23)	85.69 (9.14)	2.32	.14	.06
Mean SE Res	88.11 (5.54)	87.32 (9.83)			
Mean WASO Typ	59.25 (21.52)	89.12 (43.35)	8.78	.01	.20
Mean WASO Res	50.04 (22.62)	70.52 (33.34)			
Mean Bedtime Typ	21:04 (00:34)	20:59 (00:32)	151.62	.00	.82
Mean Bedtime Res	21:57 (00:32)	21:48 (00:35)			
Mean Wake time Typ	06:55 (00:27)	06:57 (00:30)	1.05	.31	.03
Mean Wake time Res	07:00 (00:28)	07:00 (00:30)			

Note: SD = standard deviations; TD = typically developing; TIB = time in bed; TST = total sleep time; SOL = sleep onset latency; SE = sleep efficiency; WASO = wake after sleep onset, Typ = Typical condition; Res = Restricted condition.

Table 3. 4

Means and SD for Objective and Subjective Measures of Daytime Sleepiness During

Sleep Manipulation by Group

	Mean (*SD*)	
	ADHD (*n* = 18)	TD (*n* = 18)
Objective measures		
# of Naps Res	0.82 (0.86)	0.82 (0.86)
# of Naps Typ	0.92 (0.80)	1.03 (0.80)
Mean Nap Onset Res	19.61 (1.46)	18.84 (1.52)
Mean Nap Onset Typ	18.96 (0.97)	18.86 (1.68)
Subjective measures		
Parent rated sleepiness Res (MESS)	2.83 (3.11)	1.57 (1.91)
Parent rated sleepiness Typ (MESS)	1.89 (2.72)	1.14 (2.51)
RA rated sleepiness Res (RAR)	2.19 (1.10)	2.03 (0.77)
RA rated sleepiness Typ (RAR)	1.89 (0.90)	2.17 (0.98)
Child rated sleepiness Res (CPSS)	1.61 (0.61)	1.76 (1.05)
Child rated sleepiness Typ (CPSS)	1.56 (0.50)	1.56 (0.94)

Note: SD = standard deviations; TD = typically developing; Typ = Typical condition; Res = Restricted condition; MESS = Modified Epworth Sleepiness Scale (range: 0-24); RAR = Research Assistant Report (range: 1-5); CPSS = Child Pictorial Sleepiness Scale (range: 1-5).

Table 3. 5

Means and SD for Subjectively Measured Sleep During Sleep Manipulation by Group

	Mean (*SD*)	
	ADHD (*n* = 18)	TD (*n* = 18)
Parent rated sleep duration Res (CSHQ)	5.17 (1.47)	4.72 (0.67)
Parent rated sleep duration Typ (CSHQ)	4.61 (1.09)	4.93 (1.39)
Parent rated SOL Res (CSHQ)	1.28 (0.67)	1.01 (0.02)
Parent rated SOL Typ (CSHQ)	1.39 (0.70)	1.18 (0.38)
Child rated sleep Res (CSSR)	41.50 (5.94)	39.89 (6.46)
Child rated sleep Typ (CSSR)	40.78 (5.20)	41.22 (4.41)

Note: SD = standard deviations; TD = typically developing; Typ = Typical condition; Res = Restricted condition; SOL = sleep onset latency; CSHQ = Children's Sleep Habits Questionnaire (range for sleep duration: 3-9, range for SOL: 1-3); CSSR = Child Sleep Self-Report (range: 18-54).

Table 3. 6

Means and SD for Objective Measures of Attention During Sleep Manipulation by Group

and Results for the Univariate ANOVAs for Sleep Condition

	Mean (*SD*)		ANOVA		
	ADHD (*n* = 18)	TD (*n* = 18)	F	*p*	η^2
Omissions Res	47.61 (44.54)	39.22 (45.64)	4.16	.05	.11
Omissions Typ	31.28 (25.00)	30.17 (32.70)			
Commissions Res	23.50 (4.73)	21.44 (6.05)	6.15	.02	.15
Commissions Typ	24.50 (5.69)	25.28 (4.99)			
Hit RT Res	538.17 (110.26)	521.12 (130.00)	1.55	.22	.04
Hit RT Typ	530.16 (94.61)	497.04 (118.60)			
CCTT-2 Res	76.34 (51.02)	53.64 (22.16)	2.59	.12	.07
CCTT-2 Typ	62.96 (27.11)	52.66 (24.66)			

Note: SD = standard deviations; TD = typically developing; Typ = Typical condition; Res = Restricted condition; RT = reaction time (Hit RT raw scores measured in ms); CCTT = Children's Color Trails Test (raw scores measured in s)

Table 3. 7

Means and SD for Subjective Attention Measures During Sleep Manipulation by Group

	Mean (*SD*)	
	ADHD (*n* = 18)	TD (*n* = 18)
Parent rated Inattention Res (CPRS)	19.89 (5.55)	6.44 (5.49)
Parent rated Inattention Typ (CPRS)	19.28 (5.80)	4.39 (3.43)
Teacher rated Inattention Res (CTRS)	16.56 (7.05)	6.53 (6.31)
Teacher rated Inattention Typ (CTRS)	16.22 (8.21)	5.06 (4.23)
RA rated Inattention Res (RAR)	2.22 (3.10)	1.06 (1.80)
RA rated Inattention Typ (RAR)	1.94 (2.58)	0.94 (2.01)
Child rated Inattention Res (ADHD-CSR)	5.21 (3.28)	4.94 (4.57)
Child rated Inattention Typ (ADHD-CSR)	4.89 (2.90)	3.89 (3.27)

Note: SD = standard deviations; TD = typically developing; Typ = Typical condition; Res = Restricted condition; CPRS = Conners Parent Rating Scale (range: 0-30); CTRS = Conners Teacher Rating Scale (range: 0-30); RAR = Research Assistant Report (range: 0-9); ADHD-CSR = ADHD Child Self Report (range: 0-18).

Table 3. 8

Means and SD for Objective Measures of Emotion During Sleep Manipulation by Group

	Mean (*SD*)	
	ADHD (*n* = 18)	TD (*n* = 18)
ART Positive Res	37.27 (28.96)	41.91 (15.72)
ART Positive Typ	38.41 (26.71)	39.63 (16.15)
ART Negative Res	21.19 (23.86)	28.59 (19.16)
ART Negative Typ	19.33 (17.81)	28.77 (20.29)

Note. SD = standard deviation; TD = typically developing; ART = Affective Response Task (range: 0-158 mm); Typ = Typical condition; Res = Restricted condition.

Table 3. 9

Means and SD for Subjective Measures of Emotion During Sleep Manipulation by Group and Results of the Univariate ANOVAs for Sleep Condition

	Mean (*SD*)		ANOVA		
	ADHD (*n* = 18)	TD (*n* = 18)	F	*p*	η^2
Parent rated ER Res (ERC-R)	25.72 (3.10)	27.56 (2.97)			
			.63	.43	.02
Parent rated ER Typ (ERC-R)	25.56 (3.65)	28.65 (3.87)			
Parent rated LN Res (ERC-R)	32.33 (7.16)	22.72 (6.31)			
			7.10	.01	.17
Parent rated LN Typ (ERC-R)	30.11 (7.83)	20.23 (4.48)			
Teacher rated ER Res (ERC-R)	25.23 (5.06)	27.97 (3.41)			
			1.36	.25	.04
Teacher rated ER Typ (ERC-R)	24.40 (5.91)	27.51 (3.80)			
Teacher rated LN Res (ERC-R)	28.29 (8.71)	22.97 (6.97)			
			2.42	.13	.07
Teacher rated LN Typ (ERC-R)	26.45 (7.66)	22.27 (6.28)			
RA rated mood Res (RAR)	1.94 (0.80)	2.17 (1.34)			
			1.17	.29	.03
RA rated mood Typ (RAR)	1.83 (0.92)	1.83 (0.99)			
Child rated Dysreg. Res (CEMS)	4.85 (0.82)	5.04 (1.26)			
			1.39	.25	.04
Child rated Dysreg. Typ (CEMS)	4.80 (0.97)	4.78 (0.88)			
Child rated Coping Res (CEMS)	8.39 (1.61)	8.46 (2.35)			
			1.27	.27	.04
Child rated Coping Typ (CEMS)	8.76 (1.88)	8.57 (2.57)			

Note: SD = standard deviations; TD = typically developing; Typ = Typical condition; Res = Restricted condition; ERC-R – Emotion Regulation Checklist-Revised; ER = Emotion Regulation (range: 8-32); LN = Lability/Negativity (range: 15-45); RAR = Research Assistant Report (range: 1-5); CEMS = Children's Emotion Management Scales; Dysreg. = Dysregulated Expression subscale (range: 9-27); Coping subscale (range: 12-36).

Table 3. 10

Means and SD for Objective and Subjective Measures of Cognitive Functioning During

Sleep Manipulation by Group

	Mean (*SD*)	
	ADHD (*n* = 18)	TD (*n* = 18)
Objective Measures		
STM Res	7.75 (2.23)	9.33 (2.51)
STM Typ	7.97 (2.00)	9.36 (2.64)
WM Res	5.22 (2.38)	6.03 (2.45)
WM Typ	5.56 (2.13)	6.00 (2.77)
Subjective Measures		
Parent rated Learning Res (CPRS)	13.44 (7.01)	3.89 (4.13)
Parent rated Learning Typ (CPRS)	13.11 (5.82)	2.83 (2.96)
Teacher rated Learning Res (CTRS)	7.00 (4.17)	2.00 (2.46)
Teacher rated Learning Typ (CTRS)	6.78 (4.73)	2.07 (2.43)

Note. SD =standard deviation; TD = typically developing; Res = Restricted condition; Typ = Typical condition; STM = short term memory (range: 0-23); WM = working memory (range: 0-23); CPRS = Conners' Parent Rating Scale (range: 0-30); CTRS = Conners' Teacher Rating Scale (range: 0-18).

Table 3. 11

Means and SD of Actigraphy Sleep Variables During Sleep Manipulation by Group and

Results of the Univariate ANOVAs for Sleep Condition when TST ≥ 30 min

	Mean (*SD*)		ANOVA		
	ADHD (*n* = 9)	TD (*n* = 9)	F	*p*	η^2
TIB Res	537.15 (23.77)	542.58 (40.91)	83.79	.00	.83
TIB Typ	589.30 (27.06)	596.87 (36.18)			
TST Res	439.28 (34.21)	443.49 (68.97)	175.82	.00	.91
TST Typ	502.79 (29.77)	513.44 (57.40)			
SOL Res	18.98 (7.49)	22.73 (22.23)	3.61	.07	.18
SOL Typ	26.82 (12.97)	26.01 (13.15)			
SE Res	85.27 (5.45)	85.10 (9.96)	13.72	.002	.45
SE Typ	89.16 (4.14)	90.54 (6.95)			
WASO Res	52.47 (21.06)	85.72 (38.38)	2.90	.11	.15
WASO Typ	62.80 (25.16)	98.85 (43.81)			
Bedtime Res	22:01 (0:34)	21:53 (0:38)	144.68	.00	.90
Bedtime Typ	21:15 (0:34)	21:08 (00:35)			
Wake time Res	07:01 (00:25)	07:09 (00:16)	2.42	.14	.12
Wake time Typ	06:57 (00:27)	07:03 (00:26)			

Note: SD =standard deviation; TD = typically developing; Res = Restricted condition;
Typ = Typical condition; TIB = time in bed; TST = total sleep time; SOL = sleep onset
latency; SE = sleep efficiency; WASO = wake after sleep onset, Typ = Typical condition;
Res = Restricted condition.

Chapter 4: Sleep Variables as Predictors of Treatment Effectiveness and Side-Effects of Stimulant Medication in Newly Diagnosed Children with ADHD

The manuscript based on this experimental study is presented below. The data used in this study were comprised of data from two previous studies. Readers are advised that Fiona Davidson, under the supervision of Dr. Penny Corkum, was responsible for developing the research questions, conducting background literature review, applying for and obtaining research ethics approval, coordinating the participants and paediatrician visits, completing data collection, scoring, and data analysis/interpretation. Fiona Davidson also applied for and was successful in obtaining funding to support this research. All aspects of this research were done in consultation with the dissertation committee (Dr. Benjamin Rusak and Dr. Christine Chambers). Fiona Davidson was responsible for all aspects of the writing process, and received editorial feedback from the dissertation committee.

Abstract

There is a large body of research on the impact of stimulant medication on sleep in children with attention-deficit/hyperactivity disorder (ADHD). Negative sleep side-effects are a common reason for non-adherence or for discontinuing a course of treatment. There is no published evidence, however, as to whether pre-treatment sleep can predict response to treatment and the emergence of side-effects. In this study, baseline sleep variables were used to predict therapeutic effect (i.e., reduction of ADHD symptoms) and side-effects (both sleep and global side-effects) in a sample of newly diagnosed, medication-naïve children ($n = 50$). The results of hierarchical regression analysis showed that parent-reported sleep duration prior to medication treatment significantly predicted response to treatment, independent of pre-treatment ADHD symptoms. In particular, reduced sleep duration at baseline was correlated with greater ADHD symptom reduction in response to stimulant medication. Baseline sleep features did not significantly predict global (non-sleep) side-effects; however, parent-reported problems with sleep duration and delayed sleep onset latency (SOL) at baseline were significantly correlated with increased sleep side-effects during treatment. These results indicate that baseline sleep variables may be helpful in predicting therapeutic response to medication, as well as sleep disturbance as a side-effect of stimulant medication.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a highly prevalent mental health disorder that affects approximately 5-7% of school-aged children (Wilcutt, 2012). Children with ADHD have persistent and developmentally inappropriate levels of inattention and/or hyperactivity and impulsivity that cause significant impairment in daily functioning across multiple settings such as home and school (American Psychiatric Association, 2000, 2013). Some of the main impacts of untreated ADHD on children include difficulty with academic work and a higher risk of grade retention compared to typically developing (TD) peers (Barbaresi, Katusic, Colligan, Weaver, & Jacobsen, 2007; Shaw et al., 2012). Furthermore, symptoms of ADHD often impact children's abilities to develop and maintain positive peer relationships, and many parents of children with ADHD report increased parental stress (Young & Amarasinghe, 2010). If left untreated through development, children with ADHD may continue to have difficulties with daily functioning, and may be more likely to engage in risk-taking behaviours, such as substance use (Schachar, 2009).

ADHD is a 24 h disorder, such that, in addition to daytime functioning problems, it has been strongly associated with nighttime problems, including difficulty falling and staying asleep and frequent night awakenings (Corkum, Moldofsky, Hogg-Johnson, Humphries, & Tannock, 1999; Owens, 2005). The prevalence of sleep problems in children with ADHD has been estimated to be between 25-50% (Corkum et al., 1998; Owens, 2005; Spruyt & Gozal, 2011; Yoon, Jain, & Shapiro, 2012), which is more than twice the rate found in TD children. Given that disrupted sleep can affect attention and behaviour, and that difficulties with attention and behaviour characterize ADHD, it is not

surprising that the literature suggests a link between sleep disruption and the symptoms of ADHD (Corkum et al., 1998; Owens, 2005).

Evidence-based treatments for the symptoms of ADHD include psychosocial, behavioural interventions, as well as pharmacological treatments, such as stimulant medications (Stein, Weiss, & Hlavaty, 2012). The reality is that most children are treated with pharmacological agents and are rarely provided with evidence-based psychosocial interventions (Chronis, Jones, & Raggi, 2006). Data from the National Survey of Children's Health in the United States revealed that approximately 8.8% of children between the ages of 4 and 17 years had a diagnosis of ADHD, and 6.1% were taking medication for ADHD at the time of the survey (Visser et al., 2014). The Canadian Health Measures Survey showed that 5.9% of boys, and 2.5% of girls aged 6-14 years were taking stimulant medications for ADHD (Rotermann, SanMartin, Hennessy, & Arthur, 2014). Similarly, a Canadian study revealed a significant increase in stimulant medication use in children aged 3-9 years with ADHD, from 43.4% in 2000 to 59.3%, in 2007 (Brault & Lacourse, 2012).

Research has shown that stimulant medication helps to improve daytime functioning by reducing the core symptoms of ADHD (Cockcroft, Ashwal, & Bentley, 2009; Golan, Shahar, Ravid, & Pillar, 2004; Weiss et al., 2007). The literature on stimulant medication treatment in children with ADHD suggests that due to these symptom reductions, children with ADHD also demonstrate improved performance on direct measures of academic (Faraone & Buitelaar, 2010), cognitive (Hale et al., 2011), and behavioural functioning (Schachar et al., 2008). However, not all treatments work for every individual, despite positive group outcomes (MTA Cooperative Group, 2003). In

fact, research has shown that within the first year following initiation of stimulant medication use, approximately 20-25% of children discontinue treatment, and after three years, adherence rates have fallen to approximately 50% (Charach, Ickowicz, & Schachar, 2004; Thiruchelvam, Charach, & Schachar, 2001). Given the importance of managing the symptoms of ADHD in order for children to be successful academically, behaviourally, and socially, it is necessary to understand the principal factors that impact medication adherence; namely, therapeutic effect and medication side-effects.

Many individuals with ADHD do not show an adequate therapeutic response to pharmacological treatment alone, and non-response rates can be as high as 30% (Johnston, Coghill, Matthews, & Steele, 2015; Vance, Winther, & Rennie, 2012). Researchers have identified a variety of potential moderator variables, which are defined as baseline factors that identify groups as likely to have either better or poorer response to treatment (Hinshaw, 2007). Moderator variables that are associated with a poor response to medication include increased parental symptoms of depression (MTA Cooperative Group, 2003), higher baseline severity of ADHD symptoms (Buitelaar et al., 1995; Kim Yoon, & Cho, 2010; MTA Cooperative Group, 2003), and lower child IQ (Buitelaar et al., 1995; MTA Cooperative Group, 2003), poorer performance on attention measures, and the presence of comorbid disorders such as Oppositional Defiant Disorder (Johnston et al., 2015). However, there is currently no reliable way to predict how well children will respond to medication treatment.

Poor sleep quality at baseline (defined as sleep efficiency as measured by actigraphy) has been associated with greater therapeutic response. For example, Gruber et al. (2007) found that stimulant medication use was associated with significantly improved

performance on an attention task (i.e., Continuous Performance Task) in children with ADHD who had poor sleep quality, but not in those with good sleep quality. In another study, when on medication, children with ADHD with baseline sleep duration above the group mean demonstrated more improvements in accuracy on an executive attention task compared to children with baseline sleep duration below the group mean; however, no significant associations were found between sleep quality and performance on cognitive tasks (Morash-Conway, Gendron, & Corkum, 2017). Results from these two studies suggest a relationship between pre-treatment sleep features, however the specific sleep features are different (i.e., sleep quality in one study, sleep duration in the other), and the outcomes while on stimulant medication are opposite. There is evidence from the adult literature suggesting that sleep quantity may predict treatment responsiveness, such that healthy adults with no sleep disorders whose sleep was experimentally restricted (4 h time in bed [TIB]) experienced more benefit on attention tasks from stimulant medication than those with 8 h TIB (Roehrs, Johanson, Meixner, Turner, & Roth, 2004). Together, results from these studies suggest that there may be a link between sleep quality and sleep quantity, medication use, and improved attention, however more controlled research studies are needed to determine which pre-treatment sleep feature is most important, and whether the impact is positive (i.e., improved attention), or negative (i.e., reduced attention).

There are also several lines of evidence from different clinical conditions linking sleep to treatment effectiveness. For example, poor sleep in adolescents with depression is associated with poor treatment response (Emslie et al., 2012; Manglick, Rajaratnam, Taffe, Tonge, & Melvin, 2013), and persistent sleep problems after recovery from

depression predicts relapse in adults (Franzen & Buysse, 2008). On the other hand, children with depression and insomnia are more responsive to treatment for depression than children without insomnia (Emslie et al., 2012).

Adverse side-effects of stimulant medications are the other main barrier to adherence to medication use (Charach et al., 2004). Common side-effects include sleep onset insomnia (Ironside, Davidson, & Corkum, 2010; Lee et al., 2011; Stein et al., 2012; Wilens et al., 2005), physiological symptoms (e.g., headache, stomach ache), affective changes (e.g., withdrawal, sadness), over-focusing (e.g., preoccupation with specific tasks/items), and motor tics (Charach et al., 2004). The number of treated children who experience negative side-effects from stimulant medication has been reported to range from approximately 20% to as high as 70%, and side-effects have been found to persist for years during treatment (Charach et al., 2004).

A recent study showed that high levels of subjectively reported baseline sleep problems were associated with more sleep problems on medication (Becker, Froehlich, & Epstein, 2016). Furthermore, evidence for the association between sleep disturbance and treatment of ADHD symptoms with stimulant medications is that methylphenidate promotes dopaminergic activity by blocking the reuptake of dopamine into the pre-synaptic neuron (Tarver, Daley, & Sayal, 2014). As a result, the increased levels of dopamine promote wakefulness (Monti & Jantos, 2008), which is why methylphenidate has been used as a treatment for narcolepsy (Bruck, Kennedy, Cooper, & Apel, 2005; Morgenthaler et al., 2007). This conclusion is reinforced by evidence that methylphenidate alters sleep duration and sleep onset latency (SOL) in children with ADHD (Corkum & Coulombe, 2013; Konofal, Lecendreux, & Cortese, 2010).

No study to date has examined pre-treatment sleep variables as predictors of both therapeutic effect and negative side-effects in response to medication among children with ADHD. Based on the evidence from other clinical conditions, one hypothesis of this study was that parent-reported sleep variables (e.g., sleep duration and SOL) at baseline might predict these responses to medication. The main objective of the current study was to examine whether subjective parent-reported pre-treatment sleep variables could predict treatment response and side-effects of subsequent stimulant medication treatment among children who were newly diagnosed with ADHD and were stimulant medication naïve. The research design was a randomized, within-subjects design, such that all participants experienced both the active medication and placebo conditions. In order for results to be clinically relevant and practical for use in physicians' offices, predictor and outcome variables from accessible and readily available subjective measures were used. The sleep variables of interest were parent-reported problems related to sleep duration and SOL. These sleep variables were examined to see if they predicted response to medication in terms of therapeutic effectiveness (i.e., reduced symptoms) and severity of side-effects.

Research Hypotheses

The main research question was whether baseline sleep variables based on parental reports could be used to predict effectiveness of stimulant medication in newly diagnosed children with ADHD undergoing a blinded medication trial, above and beyond variables that have been found to predict effectiveness in previous research (e.g., age, sex, full scale intelligence quotient [FSIQ], baseline ADHD symptom severity). The two hypotheses were:

1. Based on the literature, more parent-reported sleep problems at baseline (i.e., shorter sleep duration and longer SOL) would be related to increased treatment effectiveness (e.g., greater overall reduction of ADHD symptoms).

2. More sleep problems at baseline (as indicated by parent ratings), would predict increased side-effects, both sleep-specific side-effects and global side-effects, during the stimulant medication condition relative to placebo condition.

Method

Participants

Data were available for 50 children between the ages of 6 and 12 years who were newly diagnosed with ADHD. Participants had a mean age of 8.50 years ($SD = 1.73$). The sample consisted of 38 males (76%) and 12 females (24%), a ratio of ~4:1, which is representative of the sex ratio for ADHD diagnosis in the literature. The mean standard score for estimated FSIQ was 98.11 ($SD = 14.79$). Data on parental education, family income, family composition, and ethnicity were obtained, and the majority of children were Caucasian, living in two-parent homes, with community college educated parents. Family variables are summarized in Table 4.1.

Children were recruited from two previous studies that examined sleep in children with ADHD, both of which had ethical approval from the IWK Health Centre (i.e., a tertiary pediatric children's hospital), and the Capital District Health Authority (now Nova Scotia Health Authority). Both studies used similar methods and data were collected by taking advantage of clinical medication trials conducted by four community pediatricians who specialize in ADHD. The data that were used from the two previous studies included baseline sleep scores from the Children's Sleep Habits Questionnaire

(CSHQ) and baseline ADHD symptoms from the Conners' Rating Scales (see Measures section for descriptions of both measures). These measures were completed for each participant as part of the baseline data collection in both previous sleep studies, and were only used in the previous studies as a description of baseline, not as main outcome variables.

Inclusion criteria for these studies were: 1) child was 6-12 years of age; 2) child met the DSM-IV diagnostic criteria for ADHD and was diagnosed by evidence-based practice including semi-structured parent interview, parent and teacher questionnaires, and psychoeducational assessment; and 3) child was medication naïve. Most children were diagnosed using DSM-IV criteria; however, they all also met criteria as specified by DSM-5. Participants from the two studies did not differ on age, FSIQ, or on the outcome variables of interest for the current study.

Exclusion criteria for the two original sleep studies were: 1) a chronic and impairing medical illness (e.g., diabetes); 2) history of neurological impairments (e.g., epilepsy); 3) primary sleep disorder (e.g., sleep apnea, periodic limb movement disorder); 4) medication use during the past month that is likely to affect sleep; 5) crossed more than two time zones in last month; 6) regularly slept less than 8 h or more than 12 h nightly; 7) child had developed beyond pubertal Tanner stage 2 (based on parent-completed questionnaire); 8) evidence of a significant cognitive impairment; or 9) child was currently taking or had ever taken psychotropic medication. Children with ADHD who had a co-morbid diagnosis of another primary mental health disorder such as major depression or generalized anxiety disorder were also excluded. Children with ADHD were not excluded for having a learning disability (LD) given the high rates of LD in this

population. Late stage exclusion criteria included evidence on polysomnography (PSG) that was indicative of a primary sleep disorder (e.g., obstructive sleep apnea). Inclusion criteria for the current study were: 1) pediatrician determined that stimulant medication was indicated; 2) child's parent(s) decided to initiate a course of medication for their child; and 3) child's parent agreed to complete questionnaires during each condition, as well as consented to have teacher contacted to request that they complete questionnaires during the medication trial.

Measures

In order to measure children's responses to the stimulant medication trial, three parent questionnaires: 1) Conners' 3 Parent Rating Scale, 2) Children's Sleep Habits Questionnaire, 3) Side-Effect Rating Scale (parent version), and two teacher questionnaires: 1) Conners' 3 Teacher Rating Scale, and 2) Side-Effect Rating Scale (teacher version) were used in this study. These questionnaires assess children's ADHD and associated symptoms, sleep, and potential side-effects from medication.

Conners' 3 Parent and Teacher Rating Scales (CPRS-3/CTRS-3; Conners, 2008). The CPRS-3 and CTRS-3 evaluate and screen for problem behaviours in the home and school setting for children aged 6 to 18 years. The CPRS-3 has 110 items and the CTRS-3 has 115 items. These measures are commonly used in treatment trials, and are sensitive enough to evaluate changes in behaviour due to intervention, such as stimulant medication (Someki & Burns, 2009). The CPRS-3 and CTRS-3 have been reported as having excellent internal reliability with coefficient alphas ranging from .91-.94 (Conners, 2008). In this study, the indices of interest from each form were the t-scores for the inattention and hyperactivity subscales. A baseline composite score for ADHD

symptom severity was calculated by taking the mean t-scores for both scales from parents and teachers at baseline. Higher scores represented great symptom severity. Participants received both placebo and medication under blinded conditions for two weeks each. Mean composite scores for the two scales from both parent and teacher forms were calculated for the medication condition and the placebo condition. The difference in composite scores between medication week and placebo week represented the overall change in ADHD symptoms associated with medication treatment.

Side-Effect Rating Scale - Parent and Teacher versions (SERS; described in Schachar, Tannock, Cunningham, & Corkum, 1997). The SERS is a 21-item questionnaire broken down into five scales: Physiological side-effects (nine items), affective side-effects (six items), tics (three items), over-focusing side-effects (i.e., excessive pre-occupation with task or activity; two items), and rebound (i.e., increased irritability/hyperactivity after medication effect begins to wear off; one item). The SERS has been used previously in research involving medication trials, and has been successful in assessing change in side-effects over time (Schachar et al., 1997). There were two scores of interest from the SERS that were analyzed in this study, the raw score for the insomnia item ("insomnia or trouble sleeping") from the physiological scale, and the total raw side-effects score minus the insomnia item, defined as global side-effects. The raw scores for the insomnia item (range: 0-9) from parents and teachers were averaged to create a composite score defined as overall insomnia. A difference score for insomnia was calculated by subtracting the insomnia composite score during placebo condition from the insomnia composite score during medication condition. Similarly, the total raw scores for global side-effects, (range: 0-180) from the parent and teacher forms were

averaged, and the difference in composite scores between medication and placebo conditions was used in analyses.

Children's Sleep Habits Questionnaire (CSHQ; Owens, Spirito, & McGuinn, 2000). The CSHQ is a 45-item questionnaire on children's typical sleep habits, tapping into eight specific sub-domains of sleep behaviour including: Bedtime Resistance, Sleep Onset Delay, Sleep Duration, Sleep Anxiety, Night Wakings, Parasomnias, Sleep Disordered Breathing, and Daytime Sleepiness. The CSHQ has adequate psychometric properties, with test-retest reliability ranging from 0.62 to 0.79, and alpha coefficients ranging from 0.36 for the Parasomnias scale to 0.70 for the Bedtime Resistance scale in a community sample (Owens et al., 2000). In this study, the raw scores from the sleep onset delay and sleep duration subscales were used in analyses.

Procedure

Children participating in either of two larger sleep studies were given the option of attending a consultation appointment with one of four pediatricians experienced with medication trials for children with ADHD. The medication trial itself was offered as a clinical service by the pediatricians, and they had complete clinical decision-making during the trial. The pediatricians reviewed both benefits and risks associated with the medication with the families as part of their initial appointment. Along with the pediatrician, families decided whether to initiate a course of medication, and if so, the research team was then contacted. The medication that was used was extended-release methylphenidate hydrochloride (Biphentin®). Dosing was based on a weight-adjusted dose of 0.7 mg/kg, which corresponds to a moderate dose. The four-week trial consisted of two weeks of active treatment (Biphentin®) and two weeks of a placebo treatment.

Two pharmacies prepared the medication and placebo capsules, which were identical in appearance and packaging.

Each participant was randomized to complete either the two-week placebo condition or two-week treatment condition first. A prescription was then sent to the collaborating pharmacy team, who provided the de-identified prescription to the family in order to maintain blinding. All parents, teachers, children, and research staff were blind to medication/placebo order. Only the pediatrician and the pharmacy team were aware of the medication/placebo schedule for each child. Parents and teachers completed online questionnaires at the end of the first week, and again at the end of the third week. The second and fourth weeks were used as back-up weeks in the event that children were sick during the initial weeks of data collection, or teachers were not available to observe due to time off. This design ensured a representative week to evaluate the impact of medication. Each child had a follow-up appointment with the pediatrician to review the research data findings. After this appointment, the family's participation in the research study ended, and all further follow-up activities were directly with the pediatrician with no involvement from the research team.

Statistical Considerations

To determine the effect of stimulant medication on participants, repeated-measures multivariate analysis of variance (RM-MANOVA) were conducted to compare the within-participant effects of medication on symptoms of ADHD (i.e., mean composite score of CPRS and CTRS inattention and hyperactivity), insomnia side-effects (i.e., mean composite score of parent teacher insomnia ratings), and global side-effects excluding insomnia (i.e., composite scores of parent and teacher ratings of global side-effects).

Hierarchical regressions were used to examine general predictor variables (i.e., age, sex, FSIQ, and baseline ADHD severity), baseline sleep variables (i.e., parent-rated sleep duration and SOL), and whether these variables could predict the effectiveness of the medication and the side-effects of the medication. Three hierarchical regressions were run, the first examining the therapeutic effect of medication (i.e., ADHD symptom reduction), the second examining sleep side-effects (i.e., insomnia side-effects) of medication, and the third examining global side-effects. In each hierarchical regression, the general predictor variables (i.e., age, sex, FSIQ, baseline ADHD severity) were entered in the first step, and sleep variables were entered in the second step. An alpha level of .05 was used to determine statistical significance.

<center>**Results**</center>

Effect of the Medication Trial

The omnibus statistic from the RM-MANOVA examining ADHD symptoms, insomnia side-effects, and global side-effects was significant (Wilks' lambda = 0.55, F (3, 47) = 12.61, p = .000, η^2 = .45). Examination of the univariate tests revealed that ADHD symptoms (composite score of parent and teacher ratings of ADHD) were significantly higher during placebo condition compared to medication condition (F (1, 49) = 19.22, p = .000, η^2= .28). Insomnia side-effects were significantly higher during medication condition compared to placebo condition (F (1, 49) = 24.40, p = .000, η^2= .33), as were global side-effects (F (1, 49) = 7.27, p = .01, η^2= .13). In the medication condition, the mean composite t-score for ADHD symptoms was reduced by approximately one-half of a standard deviation, reflecting an improvement in symptoms. Additionally, the mean t-score for ADHD symptoms dropped from the clinically elevated

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range during placebo condition to just above the average range during the medication condition (See Table 4.2 for means and *SD*). Parent-reported insomnia was the most commonly reported side-effect during medication. Results showed that 68% of parents reported presence of insomnia during the medication condition compared to 22% during the placebo condition. The second most common side-effect reported by parents was irritability (from the affective side-effect scale) where 62% of parents reported irritability in the medication condition, however 58% of parents also reported irritability in the placebo condition. The third most common side-effect was decreased appetite (from the physiological side-effect scale) which was reported by 54% of parents during medication condition compared to 14% in placebo condition (See Table 4.3 for percentages of parent-rated side-effects).

Predictors of Symptom Reduction

The first research question was focused on symptom reduction and whether sleep variables could be used to predict how children might respond to medication. A few variables have been found to predict response to stimulant medication: age (years), sex, FSIQ, and baseline ADHD symptom severity. These general variables were included in hierarchical regression analyses as the first set of independent variables to explore whether sleep variables could predict response to treatment above and beyond these general variables. The dependent variable was the overall change in ADHD symptoms between medication and placebo conditions and was significantly predicted by the first model (i.e., age, sex, FSIQ, and baseline ADHD symptom severity; $F_{(4, 45)} = 2.75$, $p = .04$, $R^2 = .20$). The addition of the SOL score and the sleep duration score from the CSHQ into the model was significant ($F_{(6, 43)} = 3.51$, $p = .01$, $R^2 = .33$), and the change in the

F statistic was significant (F (2, 43) = 4.22, p = .02). Therefore, the sleep variables from the CSHQ significantly predicted the overall change in ADHD symptom severity above and beyond the original set of predictors. Examination of the beta coefficients revealed that baseline symptom severity of ADHD (β = .38, p = .01), and sleep duration (β = -.31, p = .05) were significantly associated with overall change in ADHD symptoms. Higher baseline ADHD symptoms were associated with greater overall change in ADHD symptoms, indicating greater response to medication. Sleep duration was inversely associated with overall change in ADHD symptoms indicating that shorter sleep at baseline (as reported by parents) was associated with a greater overall improvement in ADHD symptoms.

Predictors of Insomnia Side-Effects

The composite score for parent and teacher rated insomnia side-effects was assessed using hierarchical regression. The first set of variables (i.e., age, sex, FSIQ, and baseline ADHD symptom severity) did not significantly predict the difference between insomnia side-effects during medication versus placebo condition (F (4, 45) = 0.12, p = .98, R^2 = .01). The addition of the sleep variables from the CSHQ showed that the change in F statistic was significant (F (2, 43) = 5.37, p = .01, R^2 change = .20), however the model was not significant overall (F (6, 43) = 1.88, p = .11). Examination of the beta coefficients showed that SOL was directly correlated with insomnia change (β = 0.42, p = .02) indicating that longer SOL at baseline was associated with increased insomnia during medication compared to placebo. Sleep duration was negatively correlated with insomnia change (β = -.53, p = .003) indicating that shorter sleep duration at baseline was associated with increased insomnia during medication compared to placebo.

Predictors of Global Side-Effects

In the hierarchical regression, age, sex, FSIQ, and baseline ADHD symptom severity were the first set of independent variables, sleep duration and SOL from the CSHQ were the second set of independent variables, and the difference scores for side-effects were the dependent variables. Results showed that age, sex, FSIQ, and baseline ADHD symptom severity did not significantly predict the difference in side-effects during medication versus placebo ($F (4, 45) = 0.92$, $p = .46$, $R^2 = .08$). Results from hierarchical regression showed that when SOL and sleep duration from the CSHQ were entered into the model in the second step, the change in the F statistic was not significant ($F (2, 43) = 1.45$, $p = .25$, R^2 change $= .06$).

Discussion

The primary objective of this study was to determine whether baseline sleep variables could predict treatment effectiveness and side-effects of stimulant medication in the treatment of ADHD in newly diagnosed children. Sleep problems are a common side-effect of stimulant medication, and there are currently no reliable predictors of how a child may respond to stimulant medication. This is important given that adherence rates are poor, partly due to a lack of therapeutic effect, but often due to insomnia side-effects.

Overall, there was a significant reduction in ADHD symptoms during an acute course of stimulant medication (i.e., Biphentin®) relative to placebo. Parent-reported sleep duration problems at baseline significantly predicted overall symptom reduction, and parent-reported problems with sleep duration and SOL at baseline were associated with increased insomnia during the acute medication trial. These findings suggest that sleep disturbance at baseline is related to the effects of treatment, both positive (i.e.,

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therapeutic effect) and negative (i.e., insomnia side-effects). As such, baseline sleep needs to be considered in the clinical assessment and treatment of ADHD.

With respect to general predictors of response to medication, results showed that baseline symptom severity of ADHD was a significant predictor of symptom reduction such that higher ADHD symptom severity at baseline predicted greater overall reduction in ADHD symptoms during treatment with medication. This finding is consistent with previous literature (Buitelaar et al., 1995; Charach & Fernandez, 2013). Previous research has also found that age, FSIQ, and inattentiveness at school were significant predictors of overall symptom reduction (Buitelaar et al., 1995), whereas the data from the current study did not show this. Therefore, while these general variables may be helpful in predicting response to treatment, they are not consistently related to medication response.

In terms of side-effects, results showed that while the overall regression model was not statistically significant, there were significant correlations between parent-reported shorter sleep duration and longer SOL with larger increases in insomnia ratings between placebo and medication conditions. The findings from this study are partially consistent with one previous study on this topic that found significant associations between high levels of parent-reported sleep problems at baseline and higher levels of sleep problems on medication (Becker et al., 2016). Similar to the current study, Becker et al. (2016) examined only stimulant medication naïve children in a randomized, controlled trial. However, sleep problems were defined as a single item on a questionnaire, whereas baseline sleep variables in the current study were based on two subscales of the CSHQ. There is preliminary evidence to suggest that a relationship between baseline sleep and insomnia side-effects exists, but more studies using well-

validated measures such as the CSHQ are necessary to better understand this relationship. Given the association between the alerting effects of stimulant medications and increased insomnia while on medication, children with pre-existing sleep problems may be at even higher risk for developing sleep problems while on stimulant medications.

With respect to general predictors of insomnia side-effects, results showed that none of the general predictors (i.e., age, sex, FSIQ, baseline severity of ADHD) were significantly associated with insomnia side-effects. These findings contrast to those of Kim et al. (2010) who found that baseline attention problems were higher in children who reported sleep problems during medication.

Understanding the problems related to medication adherence is clinically important for providing best possible care for children with ADHD. Adverse side-effects such as sleep problems, loss of appetite, changes in mood, headache/stomach ache, and lack of therapeutic effect are the most common reasons for stimulant medication discontinuation documented in the literature (Charach & Fernandez, 2013; Toomey, Sox, Rusinak, & Finkelstein, 2012). Results from the current study are consistent with the previous literature on the most common and adverse side-effects. Results from a recent survey study showed that 21% of all children who had initiated medication had discontinued; 42% within the first month (Toomey et al., 2012). Other data shows that over a three year period 48% of children discontinued treatment, with 19% discontinuing in the first year (Thiruchelvam, Charach, & Schachar, 2001). Nearly half (42%) of the participants reported insomnia side-effects, however, insomnia side-effects were not different between children who continued medication versus participants who discontinued (Toomey et al., 2012).

In the current study, the therapeutic effect of medication was significant (i.e., ADHD symptoms were significantly reduced. Despite the positive therapeutics effects of medication, 68% of participants reported some insomnia side-effects during the medication condition. Given the relationship between medication discontinuation, lack of therapeutic effect, and adverse side-effects, identifying and treating factors that may play a role in predicting treatment response is extremely important prior to medication initiation. Clinicians who prescribe stimulant medications to children with ADHD should be aware of the relationship between pre-treatment sleep, therapeutic effect, and insomnia side-effects, and should share this information with families. With this knowledge, families may feel more educated, and be better prepared to deal with possible insomnia side-effects of stimulant medication.

Clinical Implications

The findings from this study are important, as many families are concerned about the impact of stimulant medications on sleep, particularly if the child has pre-existing sleep problems. Children with pre-existing sleep problems are at risk for experiencing worse insomnia side-effects during a course of stimulant medication, but are also more likely to experience therapeutic effect via ADHD symptom reduction. Therefore, families may be faced with the difficult decision of whether or not to treat the ADHD symptoms, with the possibility that insomnia side-effects may increase. Awareness of the therapeutic effects of medications even with pre-existing sleep problems may be helpful as families make decisions about treatment. Clinicians should be prepared to assist the family in weighing both the potential for positive outcomes (i.e., reduced ADHD symptoms) with the negative outcomes (i.e., insomnia side-effects). Other factors that should be taken into

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consideration include severity of pre-treatment ADHD symptoms (i.e., level of impairment experienced by child), and severity of baseline sleep problems. Depending on the severity of each, different recommendations may be made in terms of whether stimulant treatment would be a good decision for a particular child. Furthermore, there are evidence-based strategies, such as behavioural interventions, that could be implemented to address the conflicting implications of poor baseline sleep (Corkum, Davidson, Neill, & Weiss, 2014). Behavioural interventions include the implementation of healthy sleep practices (e.g., reduced caffeine during the day, reduced use of electronics before bed, comfortable sleep environment), establishment of positive and consistent bedtime routines, and faded bedtime with response cost (FBRC; Corkum, Davidson, & MacPherson, 2011). The goal of FBRC is to have children associate going to bed with falling asleep, and to create a small sleep restriction so that they are tired when they go to bed (Corkum et al., 2011). In FBRC children are put to bed, and if they are not asleep within a certain amount of time (typically 20-30 min), they are removed from bed and given a quiet, calm activity to do without falling asleep for another pre-determined amount of time (Corkum et al., 2011). After the required period of time, they are put back to bed. This process is repeated until children are able to fall asleep within the pre-determined amount of time (i.e., 20-30 min). Once child is consistently falling asleep within the set amount of time, the bedtime is moved earlier in 15-20 min increments (Corkum et al., 2011). These behavioural interventions could be implemented for children with pre-treatment sleep problems which would improve SOL, and establish positive, health sleep practices prior to medication initiation. Furthermore, they could be used while on medication to counteract the insomnia side-effects of stimulant medication.

Previous research has examined relationships between baseline variables and treatment response using a variety of subjective and objective measures. A goal of this study was for the results to be clinically useful and practical for use by physicians who commonly prescribe stimulant medications. Therefore, reliable, readily available, and quick to administer measures of sleep, ADHD symptoms, and side-effects were selected. Results suggest that subjective reports of baseline sleep may be helpful in predicting therapeutic effects of stimulant medications above and beyond general predictors, and may be related to insomnia side-effects during the acute phase of medication. Therefore, health care professionals should encourage parental monitoring of children's sleep prior to onset of medication initiation as an aid in determining effectiveness and possible side-effects.

Strengths and Limitations

This research study was designed to explore baseline sleep variables and their usefulness in predicting insomnia side-effects and therapeutic effects of medication compared to placebo during an acute course of treatment. A major strength of this study is the placebo-controlled experimental design, which allowed us to compare effectiveness and side-effects of medication during a placebo condition to those during an active medication condition. Furthermore, previous studies have explored the relationship between baseline sleep variables and response to medication, but no study has examined the additional effects of sleep duration and SOL beyond the effects of general participant characteristics.

Another strength is that the current study was designed to be clinically useful by using measures that are readily available and easy to incorporate into regular clinical

practice. Finally, the sample of children in this study was a rigorously diagnosed

medication naïve sample of children with ADHD, screened for major sleep problems

with polysomnography as well as for other serious medical conditions. Children with

common comorbid diagnoses (i.e., anxiety, depression) were excluded. Therefore, it was

possible to assess the impact of stimulant medication on ADHD symptoms without

confounding factors associated with comorbid mental health disorders or previous

treatment with stimulant medication.

This study also had some limitations. First, while the rigorously diagnosed sample

of children with ADHD was considered a strength, given that ADHD can be diagnosed in

a variety of settings, results may not generalize to all children who receive a diagnosis of

ADHD and who present to a physician's office for pharmacological treatment. Second, a

major aim was for this study to be clinically focused and relevant for health care

professionals who commonly treat children with stimulant medications. Therefore, the

ability of baseline sleep to predict therapeutic effects of medication on direct objective

measures of attention was not assessed. This would be important in a larger scale study as

there have been some relationships found between baseline sleep and direct measures of

cognitive functioning during a course of medication (Gruber et al., 2007; Morash-

Conway et al., 2017).

Future Directions

The results of this study are focused on response to medication in the short-term

and do not provide information on whether baseline sleep variables may be helpful in

predicting the longer-term response. This is an important area of research as a recent

meta-analysis showed that the negative impact of stimulant medication on sleep was

reduced the longer time the child spent on medication (Kidwell, Van Dyk, Lundahl, & Nelson, 2015). Thus, additional research examining baseline sleep variables and their relationship to long-term changes in sleep, as well as the therapeutic effect of medication is needed. Studies with larger sample sizes are needed to compare children with medication-induced sleep problems to those without medication-induced sleep problems to explore whether they differ at baseline. Finally, research comparing the treatment effectiveness of stimulant medications and insomnia side-effects of children who received sleep intervention prior to a course of medication compared to a wait-list control group would provide more insight into the relationship between pre-treatment sleep and treatment outcomes.

Table 4. 1

Descriptive Statistics and Frequencies of Available Demographic Information for

Participants

Demographic variable	*N*	Median scores
Maternal education	47	4
Paternal education	37	4
Annual income	48	6

		Frequencies
Family composition	46	Two-parent home (*n* = 37)
		Single parent home (*n* = 9)
		Caucasian (*n* = 39)
		Multi-racial (*n* = 2)
Ethnicity	44	First Nations (*n* = 2)
		Latin-Canadian (*n* = 1)

Note: Median for parental education range: 1 = some high school, 2 = completed high school, 3 = some community college, 4 = completed community college, 5 = some university, 6 = completed university; Annual family income: 1 = < 20, 000, 2 = 20, 001-30 000, 3 = 30 001-40 000, 4 = 40 001-50 000, 5 = 50 001-60 000, 6 = 60 001-70 000, 7 = ≥ 70 001.

Table 4. 2

Means and SD of ADHD Symptom T-scores, Raw Insomnia Scores, and Raw Global

Side-Effect Scores During Medication and Placebo Conditions (N = 50)

	Mean (*SD*)	
	Medication	Placebo
ADHD symptoms (CPRS/CTRS)	60.65 (8.86)	65.79 (9.77)
Insomnia ratings (SERS)	1.84 (1.63)	0.52 (1.10)
Global side-effects (SERS)	15.00 (10.70)	10.67 (8.25)

Note. SD = standard deviations; CPRS/CTRS = Conners Parent/Teacher Rating Scales
(T-scores, range: ≤ 40 - ≥ 90); SERS = Side Effect Rating Scale (insomnia side-effects
range: 0-9, global side-effects range: 0-180).

Table 4. 3

Percentage of Parent-Rated Side-Effects During Medication Versus Placebo Condition

		Condition	
	Side-effect	Medication	Placebo
Physiological	Insomnia	68%	22%
	Decreased appetite	54%	14%
	Stomach ache	48%	16%
	Headache	34%	28%
	Irritable	62%	58%
	Prone to crying	50%	32%
	Sad	32%	18%
Affective	Stares	30%	30%
	Talks less	28%	10%
	Uninterested	26%	12%
	Euphoric	8%	12%
Tics	Motor/Vocal Tics	26%	12%
Over-focused	Excessively pre-occupied	30%	18%
Rebound	Rebound	40%	16%

Chapter 5: Discussion

Overview of Findings

The goals of this dissertation were to: 1) review the literature on the impact of sleep restriction on daytime functioning in school-aged children, 2) examine the impact of experimental sleep restriction on attention, emotion, and cognitive functioning in children with attention-deficit/hyperactivity disorder (ADHD) compared to typically developing (TD) peers, and 3) determine whether baseline sleep variables (i.e., sleep onset latency [SOL] and sleep duration) could be used to predict response to medication, both therapeutic effect and negative side-effects. The main results from this dissertation are briefly summarized along with the broad research questions introduced in Chapter 1. After summarizing the main findings, issues in the field of pediatric sleep research are discussed along with general comments on the relationship between ADHD and sleep. The theoretical perspectives on the relationship between sleep and ADHD are reviewed in light of the findings of each study, and finally clinical implications and future directions are discussed.

Research Questions in the Literature

The overarching objective of this dissertation was to better understand the relationship between ADHD and sleep in school-aged children. Three broad questions about the relationship between ADHD and sleep were identified in Chapter 1 and are summarized below along with a discussion on how the findings from the dissertation addressed each of the questions.

Research question 1. What is the state of the literature on the impact of sleep in school-aged children for both typically developing and children with ADHD and

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what are gaps in this body of research? Results of the narrative review showed that there are only 10 published experimental sleep restriction papers, representing eight unique studies in school-aged children. Results also highlighted that attention is the most commonly studied domain in experimental pediatric sleep restriction and sleep deprivation studies, with at least one subjective or objective measure of attention in each of the existing eight studies that included school-aged children. Results also showed that there is mounting evidence that objectively measured attention was more impacted by cumulative sleep restriction than acute sleep deprivation. Subjectively measured attention was significantly impacted by both cumulative sleep restriction and acute sleep deprivation. Very few studies have examined the impact of experimental sleep restriction on emotional functioning. In general, parents' subjective ratings of children's emotional functioning were found to be impacted by sleep manipulation (Gruber, Cassoff, Frenette, Wiebe, & Carrier, 2012; Vriend et al., 2013). Only one study examined objectively measured emotion and found that TD children had significantly less positive affect following sleep restriction compared to sleep extension (Vriend et al., 2013). The literature on sleep restriction's impact on cognitive functioning is also quite limited to date. Memory was significantly different between cumulative sleep restriction and sleep extension in one study (Vriend et al., 2013), but no differences were found on memory tasks in another study (Sadeh et al., 2003). Neither of the two studies examining memory following acute sleep deprivation found significant changes in performance on memory tasks (Biggs et al., 2010; Randazzo et al., 1998).

These above-noted findings were critical in the design of the empirical sleep restriction study conducted as part of this dissertation research. Given that mild

cumulative sleep restriction is a more common type of sleep restriction for children and was found to be more sensitive to changes in objective measures of attention it was chosen as the design for the experimental manipulation study in this dissertation. This was also preferable from an ethical perspective as data collection occurred during the week, and there were ethical concerns with delaying bedtime for more than 1 h per night in school-aged children on school nights. In addition, no single previous experimental sleep restriction study used both objective and subjective measures of attention with multiple informants, and no previous experimental study compared sleep restriction to controlled typical sleep. Therefore, in the larger literature, it was unclear whether impact on daytime functioning was due to sleep restriction, or improvement due to sleep extension/optimization. Finally, only one previous experimental sleep study included a sample of children with ADHD, and the sample size was small ($n = 11$) (Gruber et al., 2011). Therefore, the implications of sleep restriction on daytime functioning for children with ADHD have been largely unknown to date.

Research question 2. What is the impact of mild cumulative sleep restriction on both subjectively rated and objectively measured sleep and daytime outcomes, in children with ADHD compared to healthy TD controls? Results from the experimental sleep restriction study (Chapter 3) showed that children were able to reduce their time in bed (TIB) close to 1 h in Restricted compared to Typical condition, however, total sleep time (TST) was reduced by less than 30 min. Closer examination of the other sleep variables revealed that both SOL and wake after sleep onset (WASO) were reduced during the Restricted condition which is why the reduction in TST was less than intended. Objectively measured attention was significantly impacted by sleep

restriction. Specifically, more omission and fewer commission errors were made following the Restricted condition compared to the Typical condition, indicating that the children were more inattentive and less impulsive, or demonstrated a general reduction in engagement during this task in Restricted condition. This experimental sleep restriction study was only the second study to report on objective measures of emotion, and while the null results were inconsistent with the previous study (Vriend et al., 2013), different methods were employed in the two studies (i.e., restricted sleep compared to extended sleep versus typical sleep). Consistent with previous findings, subjective ratings of emotional lability were significantly different between sleep conditions. While there are a limited number of studies available, there is preliminary evidence to suggest that mild cumulative sleep restriction may have an impact on subjectively rated emotional functioning. Parent-rated emotional lability was significantly higher following sleep restriction. The results also showed that neither TD children nor children with ADHD were significantly impacted by mild cumulative sleep restriction on either subjective or objective measures of cognitive functioning.

This study was the first experimental sleep restriction study to examine sleep restriction compared to controlled typical sleep in children with ADHD and TD children. Results showed that children with ADHD were not differentially impacted by an experimental sleep restriction compared to TD children. This finding is consistent with the one other experimental sleep manipulation study (Gruber et al., 2011) that also did not find a significant differential impact of sleep restriction on children with ADHD. However, given that children with ADHD have pre-existing problems with attention, emotion regulation, and cognitive functioning, further deterioration in these areas over

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longer periods of time could lead to greater impairment in these children compared to their TD peers.

Research question 3. Is there a relationship between pre-treatment sleep and treatment response to stimulant medication (effectiveness and negative sleep side-effects) for children with ADHD on stimulant medication? The results of the final study of this dissertation (Chapter 4) showed that there was a significant relationship between pre-treatment sleep and response to stimulant medication in a sample of medication naïve, school-aged children with newly diagnosed ADHD. In particular, parent-rated pre-treatment sleep duration significantly predicted therapeutic effect of stimulant medication for children with ADHD above and beyond known predictors (i.e., age, sex, full scale intelligence quotient [FSIQ], baseline severity of ADHD symptoms). Specifically, shorter sleep duration significantly predicted greater symptom reduction during medication condition relative to placebo. Pre-treatment problems with sleep duration and SOL as reported by parents were also associated with more insomnia side-effects during treatment compared to placebo condition. No significant associations were found between pre-treatment sleep ratings and global side-effects (e.g., affective changes, tics).

Overall, results suggested that parent-rated sleep at baseline may be helpful in predicting response to stimulant medication. There were previously very few reliable predictors of how a child may respond to stimulant medication. Furthermore, discontinuation rates for stimulant medication are high, often due to negative side-effects such as sleep problems. Sleep problems were the most common side-effect, with 68% of children experiencing insomnia during the medication condition. Evidence-based

guidelines for the treatment of ADHD with stimulant medications take into account individual pre-treatment characteristics such as age, co-morbid diagnoses, and familial attitudes to medications (Hodgkins, Shaw, Coghill, & Hechtman, 2012). Including pre-treatment sleep as one of the factors that is considered and assessed prior to medication initiation may help prescribing physicians determine initial dosing schedules of medication, and may help to better prepare families for sleep side-effect expectations.

The conflicting implication of poor pre-treatment sleep predicting both greater ADHD symptom reduction, and more insomnia is important information for clinicians. Children whose sleep problems can be treated using behavioural interventions that encourage healthy sleep practices, as well as build associations between bedtime and sleep prior to medication initiation may be better prepared to manage the negative sleep side-effects that arise, while still benefitting from the therapeutic effects of the medication.

Issues in the Field of Pediatric Sleep Research

Experimental sleep research in children is still in its infancy, and more research is needed to better understand the impact of sleep restriction on daytime functioning. This dissertation highlights three of the main difficulties with conducting, interpreting, and synthesizing the results of this research with the existing literature: 1) different types of measurement: objective versus subjective, and the differences within each, 2) different methodologies for achieving sleep restriction, and 3) current sleep recommendations in children.

Objective versus subjective measures. An important consideration when interpreting results of the narrative review, both empirical studies comprising this

dissertation, and relevant previous literature, is how sleep and daytime functioning are measured (i.e., objectively or subjectively). Experimental sleep restriction studies require the use of objective measures to ensure sleep is manipulated, and as such sleep is always measured objectively. However, across the existing studies, daytime functioning was assessed using a combination of subjective, objective, or a combination of subjective, and objective measures.

In this study, both subjective and objective measures were used, but the same results were not found for each. This is not a surprising finding, as a review of subjective and objective measures of executive functioning across 20 studies showed that only 24% of the correlations were significant between the subjective measure and objective measures, and the median correlation was only 0.19 (Toplak, West, & Stanovich, 2013). Subjective measures are observations over time, with minimal standardization with respect to where and when the measure is completed, whereas objective measures are administered in highly structured, often 1:1 settings, with the aid of an external examiner. While adherence to the standardized protocol is necessary to control for any confounding variables, the testing environment does not mimic the classroom setting or home setting from which parents and teachers take their ratings, and where children perform everyday tasks. Given the low correlations between the two types of measurement, as well as the possible theoretical differences between subjective and objective measurement of functioning, caution must be taken when interpreting results across existing sleep manipulation studies.

In the second empirical study (Chapter 4) only subjective measures of sleep, daytime functioning, and side-effects were used in order to be clinically useful with

readily available, easy to access measures. When interpreting the results of this study in relation to other studies examining the effect of stimulant medication on sleep and daytime functioning, it is necessary to note how sleep and daytime functioning were measured (i.e., objectively versus subjectively). Results showed that subjective ratings of pre-treatment sleep predicted improvement in subjective ratings of children's symptoms, but there is also evidence to suggest that subjective ratings of pre-treatment sleep may be related to objective measures of daytime functioning (Gruber et al., 2007; Morash-Conway, Gendron, & Corkum, 2017).

In summary, neither objective nor subjective measures are necessarily better than the other, but they tap into different aspects of functioning, and reflect different time frames. Therefore, it is important for researchers to choose the type of measure based on the research question, and for consumers of the knowledge to be aware of the differences.

Methodologies for experimental sleep restriction. As discussed in the narrative review (Chapter 2 of this dissertation), there are different methods for experimentally manipulating sleep: acute sleep deprivation, cumulative sleep restriction, sleep extension, and sleep optimization. Further, the impact of the manipulation can be examined between groups or within groups and functioning can be compared between manipulated sleep conditions, or can be compared to baseline functioning. For acute sleep deprivation, the amount of deprivation used in the school-aged children literature was either 4 h TIB (Fallone et al., 2001) or 5 h TIB (Biggs et al., 2010; Randazzo et al., 1998). In these three studies, daytime functioning following sleep deprivation was compared to optimized sleep (i.e., 10-11 h TIB). While these experimental designs allow for examination of functioning following an acute sleep deprivation, the generalizability of these results is

limited as it is uncommon for a child to only sleep for 4-5 h per night. The National Sleep Foundation (NSF) Sleep in America poll in 2014 revealed that only 8% of children were getting 7 h or less of sleep per night (NSF, 2014). While no data were available to determine how many school-aged children receive 4-5 h per night, it must be fewer than 8%. Results from the poll indicated that 69% of children were getting 9 h or more, and 23% were getting ~8 h per night (NSF, 2014), providing evidence that mild cumulative sleep restriction is a more common type of restriction in children.

All published cumulative sleep restriction studies compared the sleep restricted condition to either optimized sleep (Fallone et al., 2005), extended sleep (Gruber et al., 2012; Vriend et al., 2013), or baseline sleep (Gruber et al., 2011; Sadeh et al., 2003). The sleep restriction study in this dissertation (Chapter 3) was the first to compare cumulative sleep restriction to children's *controlled* typical sleep (i.e., a prescribed sleep schedule based on their habitual sleep habits). As highlighted in Chapter 3, the problem with comparing to extended or optimized sleep is that it is unclear whether daytime functioning is negatively impacted because of sleep restriction, or improved due to extended or optimized sleep. Therefore, the results of this study and those of previous studies cannot be directly compared, given that the comparison groups are different. Based on the results of the sleep restriction study of this dissertation, it seemed that baseline sleep may play a role in how much sleep restriction or sleep extension impacts daytime functioning, and could impact whether sleep could be extended at all. Children who are already sleep restricted at baseline may show more benefit from optimized or extended sleep than children who are sleep satiated.

This hypothesis also relates to Chapter 4 such that children with ADHD who were more sleep restricted at baseline had a larger therapeutic response to stimulant medication, and more negative sleep side-effects. The study of habitual baseline sleep pre-manipulation and pre-treatment may play an important role in interpreting results with respect to daytime functioning.

Sleep recommendations in children. One of the major problems in the pediatric sleep field is the lack of empirical evidence for sleep duration recommendations, and what the optimal sleep duration is for children. A recent review of the literature suggested that most pediatric sleep recommendations are based on a combination of expert opinion, research, and consensus evidence, but there are no data describing the process by which the recommendations are made (Matricciani, Blunden, Rigney, Williams, & Olds, 2013). Matricciani et al. (2013) highlighted that the most commonly cited research that does exist on sleep recommendations was conducted over 30 years ago, in a small sample of children in a summer camp environment (Carskadon et al., 1980).

They also suggested that the existing experimental sleep manipulation studies can help to inform about children's sleep needs, but the studies that compared sleep restriction to optimized sleep (i.e., 10-11 h) assumed that children sleeping 10-11 h were sleep satiated (Matricciani et al., 2013). This is problematic for two reasons: first, 10-11 h is not based on empirical data, and second, sleep is an appetitive behaviour, and just because children sleep more does not necessarily mean that they need more sleep (Matricciani et al., 2013). It remains unclear how much sleep is actually needed for optimal daytime functioning. Despite concerns raised in Matricciani et al. (2013), the National Sleep Foundation released new sleep recommendations in 2015 with ranges for

recommended sleep, ranges that may be appropriate, and ranges that were not recommended (Hirshkowitz et al., 2015). These recommendations were based upon the decisions of a multidisciplinary expert panel and the results of a systematic review of the literature. The issues raised in Matricciani et al. (2013) were not addressed as the sleep duration recommendations continue to be based on recommendations presented repeatedly in the literature, rather than evidence of a dose-response relationship between sleep duration and daytime outcomes (Matricciani et al., 2013).

This issue of non-empirically supported sleep duration recommendations has implications for sleep manipulation research, particularly for designs that compare restricted sleep to optimized sleep, as well as implications for determining clinical sleep recommendations for families based on the results of these manipulation studies. The design of the sleep restriction in this dissertation was based on children's habitual sleep; therefore, the results are not reliant upon a specific sleep duration recommendation, but rather focus more generally on the impact of a mild cumulative sleep restriction of 1 h delayed bedtime. Furthermore, given that the design of this dissertation was based on children's habitual sleep habits, it took into account the individual variability in sleep need that may exist between children.

General Comments on the Relationship Between ADHD and Sleep

This dissertation was focused on better understanding the relationship between ADHD and sleep problems. Findings from the narrative review showed that ADHD has been largely understudied with respect to experimental sleep manipulation. There is a common belief that children with ADHD have different sleep than TD children. Although some individual studies have found significant differences between sleep in children with

ADHD compared to TD children, recent meta-analyses, and the results of this dissertation do not support this conclusion (Corkum & Coulombe, 2013; Cortese et al., 2009; Cortese et al., 2006; Sadeh et al., 2006). Furthermore, the results of this dissertation, along with the one previous study examining sleep restriction in TD children compared to children with ADHD (Gruber et al., 2011), showed that children with ADHD were not differentially impacted by mild, cumulative sleep restriction.

Theoretical Perspectives on the Relationship Between ADHD and Sleep

The circadian delay hypothesis. The circadian delay hypothesis suggests that children with ADHD have delayed sleep onset due to a delayed evening increase in melatonin release (Van der Heijden et al., 2005). The children that participated in the studies comprising this dissertation were free of any medications that might impact sleep (e.g., stimulant medication, melatonin). Our results showed that at baseline, the sleep of both children with ADHD and TD children was the same whether measured objectively via actigraphy or subjectively with questionnaires. Consistent with the literature, actigraph data showed that the means for TIB, TST, SOL, SE, bedtime and wake time were not statistically different between groups (Corkum & Coulombe, 2013). Therefore, the findings from this study show that the circadian delay hypothesis does not fully explain the relationship between ADHD and sleep.

A recent systematic review revealed that while there is some evidence that children with ADHD show delayed sleep onset delay due to delayed melatonin release, there are only 13 studies that have objectively assessed circadian rhythms in children with ADHD, and results are inconsistent overall. Furthermore, results are confounded due to a mix of participants with ADHD, some of whom have co-morbid mental health

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disorders, and some of whom are medicated with methylphenidate (MPH; Coogan &

McGowan, 2017), which has resulted in a significant phase delay and reduction in

circadian amplitude (Ironside et al., 2010). Therefore, the relationship between delayed

sleep onset in children with ADHD may be more related to the effects of stimulant

medication delays, rather than delayed melatonin release.

The nocturnal activity hypothesis. The nocturnal activity hypothesis suggests

that ADHD is a 24 h disorder with increased motor activity during sleep as well as during

the daytime hours (Corkum & Coulombe, 2013; Hvolby, 2015; Konofal et al., 2010).

Support for this hypothesis comes from research showing that children with ADHD have

more motor activity during sleep (Konofal et al., 2001), and intervention research in

adults that shows that while MPH can help manage daytime ADHD symptoms, MPH

negatively effects sleep duration and SOL, but also reduces nocturnal motor activity and

improves sleep quality (Kooij et al., 2001). The results from the studies comprising this

dissertation showed that no significant differences were found between sleep in children

with ADHD versus TD children, either at baseline, or during the sleep manipulation.

Periodic limb movements were not examined, and as such this cannot be ruled out

completely.

The hypoarousal hypothesis. The hypoarousal hypothesis suggests that the

relationship between ADHD and sleep is explained by neurobiological processes that

occur in the pre-frontal cortex (Yoon et al., 2012), and that symptoms of ADHD may be

symptoms of lowered arousal/alertness, manifesting as inattention. Furthermore,

excessive motor activity is a strategy used to help maintain daytime arousal (Brown &

McMullen, 2001). Some previous research has shown that children with ADHD are

sleepier than TD children (Golan et al., 2004; Lecendreux et al., 2000; Cortese et al., 2006), which provided evidence for this hypothesis. Consistent with one previous study (Prihodova et al., 2010), the results from the current study did not show that children with ADHD were sleepier than TD children based on MSLT data. In general, the results from this dissertation showed that there does not seem to be a unique relationship between sleep and ADHD in rigorously diagnosed, medication naïve children with ADHD. However, given the daytime difficulties of children with ADHD, and the paucity of experimental sleep restriction studies including this population, more research with medication naïve children, without co-morbid mental health disorders is needed to further examine the impact of reduced sleep on daytime functioning

Strengths and Limitations

The studies comprising this dissertation had several strengths. The narrative review (Chapter 2) comprehensively synthesized the available literature and informed the design for the experimental sleep restriction study. The first empirical study (Chapter 3) employed an experimental within- and between-subjects design to assess the impact of mild cumulative sleep restriction compared to controlled typical sleep. The within-subjects design was used to account for some of the problems with between-subjects designs. Furthermore, the addition of the controlled typical sleep week in comparison to restricted sleep, was a strength of this study as it allowed for the examination of whether changes occurred in daytime functioning due to sleep restriction rather than changes due to sleep extension as in previous studies (Sadeh et al., 2003; Vriend et al., 2013).

The decision to use a mild cumulative sleep restriction was also a strength as it represents a common and enduring pattern of sleep restriction experienced by many

school-aged children. Another strength was the use of both objective and subjective measures, which allowed for examination of each domain of interest in multiple ways. Additionally, subjective reports were based on multiple informants to obtain information across several settings in which the child was observed. Both empirical studies in this dissertation included rigorously diagnosed medication naïve children with ADHD which was important to control for previous treatment with stimulant medications and comorbidities. The second empirical study (Chapter 4) was designed to be clinically useful and therefore the measures included were ones that are easily and freely accessible. The medication trial was double-blind, and placebo-controlled, to allow for more control, and examination of true effects of medication.

Despite several strengths, there are some limitations to consider. Both studies were conducted in the short-term, and therefore, questions remain as to the long-term outcomes of cumulative sleep restriction, and the long-term predictive ability of baseline sleep for response to medication. Experimental sleep restriction studies are extremely time consuming for both researchers and families. Adding additional visits to the sleep lab, or even asking families and teachers to collect at home or at school data, or manipulate sleep in the long term would be adding both time and financial burden. Therefore, having an additional visit would have been logistically troublesome. The current design was difficult enough for families to commit to, as participants spent at minimum six weeks in the study (i.e., four weeks in active data collection, and two weeks in recovery/washout periods), with three separate 24 h visits to the sleep lab. Families of children with ADHD also had two additional weeks of washout, plus four weeks of the medication trial, and two visits to a pediatrician.

These considerations also lead to another limitation, which was the modest

sample size in the experimental sleep manipulation study (Chapter 3). Due to some of the

difficulties with experimental sleep restriction, data for some children were not analyzed

as they did not meet the 30 min less TIB sleep restriction criteria used in previous

research (Sadeh et al., 2003; Vriend et al., 2013). Furthermore, some children were able

to make up for restricted sleep in their typical sleep condition by reducing both SOL and

WASO, thereby limiting the effect of the sleep restriction. With a modest sample size to

start, there were few participants remaining for secondary analyses on children who were

able to effectively reduce their TST.

Finally, the sample of children with ADHD comprised those who were rigorously

diagnosed in specialized clinics and private psychological practices using stringent

criteria. In addition, all children were medication naïve and screened for both pre-existing

sleep problems as well as comorbid mental health disorders. Therefore, the results may

not generalize to all children with ADHD that are seen by health professionals for sleep

problems, or for medication consultations. More research is needed to include the larger

spectrum of children presenting with ADHD and other comorbid, mental health

diagnoses.

Future Research Directions

Experimental sleep restriction studies in children show that some daytime

functions are negatively impacted by sleep restriction and other daytime functions are

positively impacted by sleep extension, yet how much sleep is needed remains unknown.

Results from the second empirical study (Chapter 4) suggested that subjectively rated

sleep may be useful for predicting response to medication for children with ADHD.

These results rely less upon the idea of optimal sleep, but rather focus on parental perception of sleep, and how this relates to effect of medication. The results from both studies suggest that understanding baseline sleep may be an important factor in both sleep manipulation and treatment with stimulant medication in children with ADHD. Furthermore, as previously discussed, there are complicating factors when conducting experimental sleep research that can significantly impact outcomes. In particular, TIB was the sleep variable that was manipulated in the experimental sleep manipulation (Chapter 3), as TIB can be externally controlled by setting bedtime and wake times. On the other hand, TST cannot be externally controlled, a point that was highlighted in the results of this study whereby participants had reduced SOL and WASO in the Restricted condition, demonstrating a physiological adaption to the sleep restricted state. This unintended adaptation thus confounded the original goals of this research.

The literature on sleep and medication response is sometimes confounded by external variables such as how ADHD was diagnosed, previous medication use, and comorbid mental health disorders. Future research on the relationship between ADHD and sleep should continue to focus on children with ADHD who are medication naïve and without comorbid mental health disorders. More experimental sleep manipulation studies with children with ADHD are needed to better understand how sleep and symptoms of ADHD are related, particularly how cumulative sleep restriction over the long term impacts daytime functioning. Furthermore, intervention research with pre-treatment sleep interventions for children considering a course of stimulant medication may help to treat sleep problems before they are exacerbated by medication, thus increasing adherence to medication, and helping make ADHD symptoms and side-effects more manageable.

Clinical Implications

The literature on pediatric experimental sleep restriction is starting to grow, and together, the results from the sleep manipulation study in this dissertation (Chapter 3), along with previous findings suggest that changes in attention are found following sleep restriction and extension. Furthermore, results from the second empirical study (Chapter 4) suggested that children's pre-treatment sleep may provide clinically useful information when considering treatment with stimulant medication. More research is needed to corroborate the findings of this dissertation; however, these results point to the need for assessing sleep in school-aged children as part of clinical assessments. Given that this area of research is still small, care needs to be taken in the research field not to overstate or understate findings.

The results from both empirical studies (Chapters 3 and 4) add to the knowledge on the relationship between sleep and daytime functioning, with particular focus on children with ADHD. This was only the second study of experimental sleep restriction in children with ADHD. Results showed that baseline sleep did not differ between children with ADHD and TD children, and children with ADHD were not differentially impacted by sleep restriction.

In addition, results from both empirical studies in this dissertation suggested that baseline sleep seems to be important, and baseline sleep assessment may be useful for determining whether families see sleep as a problem, and interventions focused on the specific problems can be provided. With a measure of baseline sleep, change from baseline can be assessed during any sleep interventions, or during a course of stimulant medication. Generally, it may be important to focus on promoting empirically supported

healthy sleep habits such as consistent bedtime routines, exercise/outdoor time during the day, limited caffeine before bed, positive bed/sleep association, limited electronics before bed and in the bedroom (See *ABCs of SLEEPING*; Bessey, Coulombe, & Corkum, 2013). Practicing and establishing healthy sleep habits in childhood may encourage the natural opportunity for optimal sleep for that individual, and may act as a preventative intervention for sleep problems. Healthy sleep habits may set children up with the knowledge and skills required to manage sleep problems that may arise during a course of treatment for ADHD, and may mitigate the negative impact of stimulant medications on sleep. Future researchers should explore the possible benefits of such a pre-treatment sleep intervention on children preparing to initiate a course of stimulant medication.

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