THE RELATIONSHIP BETWEEN SLEEP AND WORKING MEMORY IN SCHOOL-AGED CHILDREN

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Abstract

There is increasing evidence to suggest that sleep problems are associated with working memory (WM) difficulties in school-aged children. However, research to date has been minimal (particularly in clinical populations of children) and results inconclusive. Moreover, very few studies investigating the relationship between sleep and WM in school-aged children have been theoretically driven. Consequently, there has been little exploration of the impact of sleep on the multiple components of WM, or the biological mechanisms driving the relationship between sleep and children’s WM. Thus, the aim of this thesis was to provide a systematic investigation of the relationship between sleep and WM, and the possible mechanisms underlying the relationship in school-aged children. The current thesis focused on two possible mechanisms by which sleep might impact on children’s WM performance – daytime sleepiness (secondary to sleep disturbance) that adversely affects children’s vigilance, or executive dysfunction as a result of sleep-related neuronal injury primarily within the prefrontal cortex.

The first study reported in this thesis (Chapter 4) investigated the relationship between sleep and verbal and spatial WM performance in 78 healthy, typically developing school-aged children aged 7 to 11 years. Sleep measures included parental-report of sleep quality and snoring. WM was assessed using measures of domain specific (verbal and spatial) WM and storage capacity, and a domain general measure of processing speed. It was argued that if sleep remained predictive of WM performance following the control of individual differences in processing speed, storage capacity and daytime sleepiness, this would suggest that sleep was impacting on the executive component of WM. This would implicate a sleep-related insult to the prefrontal cortex as the mechanism underlying the relationship between sleep and WM. Results revealed no significant relationship between any of the sleep and WM measures. However, one
limitation to Study 1 was a lack of variability in our sleep parameters, with the majority of parents reporting minimal sleep disturbance in their children.

To address this issue, Study 2 investigated the relationship between sleep and WM performance in 237 children (aged 6 to 11 years) with neurological conditions, as this population of children are reported to have increased sleep problems and WM difficulties relative to typically developing children. The methodology was similar to Study 1. While no relationship was found between snoring and WM, results from Study 2 revealed an association between poor sleep quality and verbal WM difficulties, above and beyond the influence of processing speed, storage capacity, and daytime sleepiness. This suggested that sleep was impacting on an executive component of WM, thus supporting sleep-related prefrontal injury as a mechanism underlying the sleep and WM relationship. However, spatial WM was not associated with any of the sleep measures, arguing against a global prefrontal injury.

Study 3 focused on the relationship between sleep and working memory difficulties in children born very preterm. Children born very preterm were of particular interest as recent research has demonstrated an association between sleep and the cognitive performance of children born very preterm, not evident in children born to term. Following on from Study 2, the association between sleep and verbal WM was investigated in 89 children (aged 6-7 years) born very preterm. As predicted, sleep quality was associated with verbal WM performance above and beyond the influence of processing speed, storage capacity, and daytime sleepiness. Again, no relationship was found between snoring and WM, suggesting that verbal working memory performance may be more vulnerable to the effects of poor sleep quality than those of habitual snoring. The aim of the second part of the study was to examine the impact of poor sleep on executive functioning more directly. Executive functioning was assessed in 43 children born very preterm and 48 children born to term aged 6 to 9 years, using a
measure of abstract reasoning. Parental report of overall sleep problems was collected. As predicted, the results revealed a significant effect of sleep problems upon the executive functioning of children born very preterm, whereas no effect was evident in children born to term. These findings further implicate executive dysfunction as a possible mechanism by which sleep adversely impacts upon WM in children. The theoretical and clinical implications of the findings of this thesis are discussed in the General Discussion.
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Statement of Original Authorship and Candidate Contribution

The work contained in this thesis has not been previously submitted to meet requirements for an award at this or any other higher education institution. Each of the studies in this thesis was designed by the candidate in collaboration with her supervisors, Dr. Donna Bayliss and Associate Professor Romola Bucks. The application for data, ethical approval, statistical analysis and interpretation, and preparation of manuscripts were conducted by the candidate. The manuscripts were written by the candidate, with guidance provided by her supervisors and co-authors.

Signature: ____________________________

Date: ____________________________
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Preface

Working memory refers to one’s capacity temporarily to store and manipulate task relevant information required to perform complex, cognitive tasks such as critical thinking, learning, and comprehension (Baddeley & Hitch, 1992, Biggs et al., 2011). Working memory has become a highly influential construct within such fields as cognitive psychology, neuroscience, and developmental psychology (Andrade, 2001). The application of the working memory construct in these fields has generated new hypotheses that have helped in the understanding of both typical and atypical functioning in children and adults (Andrade, 2001). One central, theoretical issue arising from current research is the nature of the factors that underlie individual differences in working memory performance in children (Miyake, 2001). One factor that has received minimal attention, which may be contributing to individual differences in performance, is sleep.

This thesis aimed to investigate the relationship between sleep and working memory performance in school-aged children. Moreover, the thesis aimed to explore plausible biological mechanisms by which sleep might impact upon school-aged children’s working memory performance. Measures of processing speed and storage capacity were included to account for individual differences in working memory performance associated with the two components, while measures of daytime sleepiness and executive functioning were included to investigate the mechanisms by which sleep might impact upon children’s working memory (and cognition in general).

The sleep and working memory relationship was explored across three, different populations of children: typically developing children, children with neurological conditions, and children born very preterm. We chose to investigate sleep and working memory in both typically developing children, and two clinical populations of children, based on evidence suggesting many children with neurological conditions and children...
born very preterm are at increased risk of sleep and working memory difficulties. As such, these children demonstrate greater variability in working memory performance and sleep parameters than would be observed simply by investigating the relationship in typically developing children alone. By exploring sleep and working memory in typically developing children and two clinical populations of children, we were able to obtain a broader understanding of the relationship in school-aged children. Further, by investigating the relationship in children with neurological conditions and children born very preterm, it was hoped results from the current research would assist in earlier diagnosis and more effective interventions for working memory difficulties in vulnerable populations of children.

To the best of the current researcher’s knowledge, no other study has investigated the relationship between sleep and working memory in children born very preterm, nor has any study investigated the relationship transdiagnostically across children with neurological conditions, with existing studies limited to the investigation of sleep and working memory in children with autism, epilepsy, or attention deficit hyperactivity only. Further, the current research is also novel in its approach to the investigation of sleep and working memory. Throughout this thesis, the assessment of working memory entailed a number of independent measures of cognitive abilities demonstrated to contribute to working memory performance in children, which no other study investigating children’s sleep and working memory has included. Our assessment of working memory is based on studies demonstrating the separability of verbal and spatial working memory (e.g., Alloway, Gathercole, & Pickering, 2006), and the contribution to performance by three subcomponent of working memory – processing speed, storage capacity, and an executive coordinating component (central executive) (e.g., Bayliss, Jarrold, Gunn, & Baddeley, 2003). Including independent measures of the working memory components implicated in children’s performance by past research
enabled the current research to pinpoint specifically where working memory performance is breaking down, which is extremely useful for clinicians when designing treatment plans.

This thesis is presented as a collection of papers in a format suitable for publication. At the time of submission, Chapters 5 and 6 were under review at the Journal of Child Neuropsychology: A Journal on Normal and Abnormal Development in Childhood and Adolescence, and Chapter 4 had been prepared for publication. Chapters 1, 2, and 3 present a literature review which provides a rationale for the investigations presented in this thesis. Chapter 7 presents a discussion of the findings in relation to past research, followed by the theoretical and clinical implications of the current research.
Chapter 1:

Working Memory
The Working Memory Model

The term working memory is used to describe a flexible, mental workspace in which to temporarily store and manipulate information in order to support ongoing performance on complex cognitive activities (Baddeley, 1992). Given that working memory plays an essential role in learning and academic achievement, understanding children’s working memory is crucial for neuropsychologists and other academic and professional groups (Alloway & Alloway, 2010; Gathercole, 1998). While there are a number of theoretical accounts of working memory, the most influential model of working memory, and the model that has guided the current research, was proposed by Baddeley and Hitch (1974).

Baddeley and Hitch (1974; Baddeley, 1986) proposed a multicomponent model of working memory that comprised an attentional control system – the central executive – assisted by two slave systems: the phonological loop (also known as the articulatory loop), which was thought to hold and manipulate verbal information; and, the visuospatial sketchpad, which was thought to perform a similar action with visual and spatial information. The model posits that working memory is limited in its capacity, and acts simultaneously to store and manipulate information used to support ongoing cognitive activities. The phonological loop is thought to comprise a phonological short-term store and a subvocal rehearsal system. The phonological store holds memory traces in a phonological code, for a matter of seconds, before they decay, while the subvocal rehearsal system refreshes decaying memory traces held in the phonological store, and recodes information from other modalities into phonological codes (verbal speech). The visuospatial sketchpad is also comprised of a short-term store, thought to hold visual and spatial images and, possibly, kinaesthetic components. Like the phonological loop, material is subject to rapid decay and some form of rehearsal and maintenance is thought to take place (Henry, 2012). Baddeley and Hitch’s (1974) model was updated in
1986, and again in 2000, in order to address the role of the central executive and incorporate the episodic buffer: described below.

Relative to the above components of working memory, the central executive is less well understood. It was initially based on the supervisory attentional system proposed by Norman and Shallice (1986), whereby attentional control is required to overcome automatic, routine control in the event of novel situations (Baddeley, 2003). The central executive is thought to be a modality-free system which directs, allocates, and controls attention within the working memory system. It provides high-level executive control during novel situations that require new behaviours or approaches (Henry, 2012). An additional component, the episodic buffer, was introduced to address the question of how information from long-term memory is linked to information from the two slave systems (Baddeley, 2000). Baddeley (2000) proposed that the episodic buffer temporarily stores chunks of information received from the phonological loop and the visuospatial sketchpad, along with information from perception and long-term memory (Baddeley, Allen, & Hitch, 2010). These chunks of information are then thought to be available to conscious awareness (Baddeley et al., 2010).

**Measuring Working Memory in Children**

The basic requirement of any working memory task is that the participant must be called upon both to store and process (manipulate or transform) information temporarily (Parker & Payer, 2006). That being said, there are a number of different methods used across studies to assess working memory. Moreover, assessment of the individual components that contribute to working memory also requires different types of tasks.
Measurement of the Phonological Loop

Verbal short-term memory measures are commonly used to assess the capacity of the phonological loop. These are speech-based, span tasks that require the participant to repeat back, verbatim, a string of numbers, letters, or words. A person’s span is taken to be the longest string of items that the participant can correctly recite back. While conventional verbal span tasks (e.g., digit span tasks) are reliable and easy to administer, a criticism of these tasks is that it is difficult to rule out the influence of long-term memory due to the familiarity of the items used in the tasks and, as such, it is difficult to obtain a pure measure of phonological storage capacity (Dehn, 2011). A number of non-word repetition tasks have been designed to avoid interference from long-term memory. These tasks require the repetition of novel phonological forms, so as to reduce the availability of long-term lexical knowledge as backup to aid in their recall (Dehn, 2011). However, these tasks too have been criticised as tapping other cognitive abilities including long-term lexical knowledge (some non-words resemble real words), phonological sensitivity, and speech production (Henry, 2012).

Measurement of the Visuospatial Sketchpad

The capacity of the visuospatial sketchpad is assessed by a number of imagery, visual, and spatial tasks. Most tasks focus either on spatial or visual short-term memory. Spatial short-term memory measures are typically based on the ‘Corsi Block Tapping’ task (Milner, 1971). In this task, an administrator taps a sequence of blocks located on a board, and the participant is required to reproduce the given sequence by tapping the blocks in the same sequence. Similar to verbal short-term memory tasks, span is measured as the longest sequence that is correctly produced by the participant. Visual short-term memory is typically assessed using visual pattern span tasks (e.g., Wilson, Scott, & Power, 1987), whereby a matrix or grid is presented with certain cells filled to
form a pattern. The grid or matrix is then removed from sight, and the participant’s task is to reproduce the pattern. The number of filled cells increases with every correct pattern produced by the participant, with span taken to be the number of filled cells in the last pattern remembered correctly. These pattern tasks are differentiated from spatial tasks in that the spatial information to be remembered is static, and there is visual detail to recall (Mammarella, Pazzaglia, & Cornoldi, 2008). The challenge, when assessing visuospatial short-term memory, is to ensure the task minimises the use of verbal strategies to recode visuospatial information.

**Measurement of the Central Executive**

Backward span tasks are commonly used to assess the central executive component of working memory. In these tasks, a string of items is presented to the participant, who is asked to repeat back the string of items in reverse order. Span is measured in the same way as short-term memory span tasks, based on the longest, correctly produced sequence. The items can be presented verbally, such as in a digit span backwards task, or spatially, such as when the Corsi Block Tapping task is presented for backwards recall. Other tasks designed to tap the central executive include n-back tasks (where the participant must compare the current stimulus to one presented n items prior in the sequence), and letter-number sequencing tasks. Unlike short-term memory span tasks, that require the storage of information alone, backward span tasks require the simultaneous processing (reordering test items) and storage of information. This simultaneous storage and processing is assumed to place direct demands on the central executive (Henry, 2012).

Another task that is frequently used to assess the central executive component of working memory is the complex span task. A commonly used complex span task is the reading span task (Daneman & Carpenter, 1980), which requires participants to read and comprehend sets of sentences while having to retain the final word of each sentence for
later recall. The task is posited to measure the central executive component of working memory in that it requires the coordination of processing and storage abilities (Daneman & Carpenter, 1980). A person’s span is measured as the longest list of recalled ‘end of sentence’ words a participant can accurately recite.

Two popular test batteries that were designed to reflect the three major components of Baddeley and Hitch’s working memory model listed above are the Working Memory Test Battery for Children (WMTB-C; Pickering & Gathercole, 2001) and the Automated Working Memory Assessment (AWMA; Alloway, Gathercole, & Pickering, 2004; 2007). Both test batteries include measures that assess the capacity of each of components of Baddeley and Hitch’s working memory model (the phonological loop, visuospatial sketchpad, and the central executive). For example, the WMTB-C includes Listening recall, Counting recall, and Backwards digit recall (central executive), Digit recall, Word list matching, Word list recall, and Non-word list recall (phonological loop), and Block recall and Mazes memory (visuospatial sketchpad). The AWMA is a computerised assessment battery. Most of the AWMA subtests are modified versions from the WMTB-C (e.g., Digit recall, Word list recall, Non-word list recall, Listening recall, Counting recall, Backwards digit recall, Block recall and Mazes memory); however, the AWMA also contains unique subtests including Dot matrix, Odd one out, Mr X, and Spatial span. Of note, the AWMA is the first standardised tool for non-specialist assessors such as classroom teachers to screen their pupils for significant working-memory problems quickly and effectively.

**Measurement of the Episodic Buffer**

Due to a lack of understanding of the nature of the episodic buffer, there are no widely agreed measures for assessing this working memory component. Henry (2012) suggests the likely tools to assess the episodic buffer are binding tasks, given the role of the episodic buffer in working memory is to bind information from the other
components and long-term memory (for a review, see Henry, 2012). The critical requirement of these tasks is the binding of information from different sources, modalities, and/or working memory components into meaningful memory representations.

**Experimental Evidence Demonstrating the Separability of the Working Memory Components**

Evidence to support the separability of the components of working memory comes from experimental research. Dual tasks were used by Baddeley and Hitch (1974) to demonstrate that short-term memory and working memory are separable structures. Dual tasks involve a participant performing two tasks simultaneously, and examining the cost to performance of combining the tasks. Baddeley and Hitch (1974) had participants perform complex cognitive tasks thought to rely on working memory, while simultaneously performing a second task aimed at reducing the availability of the participant’s short-term memory capacity. Reducing the capacity of short-term memory had only a small effect on the complex cognitive tasks, which was inconsistent with the idea of a unitary, short-term memory system that doubled as a working memory system. Several studies using similar, experimental designs (e.g., dual or interference tasks) have also demonstrated the separability of verbal and spatial storage capacity, while at the same time establishing a general resource processing component (e.g., Klauer & Zhao, 2004; Miyake, Witzki, & Emerson, 2001). However, the nature of the processing component remains vigorously contested, with some researchers arguing for the separability of the processing aspects of working memory (e.g., Mackintosh & Bennet, 2003; Pimperton & Nation, 2010; Shah & Miyake, 1996). For example, Shah and Miyake (1996) proposed that the distinction between verbal and spatial working memory goes beyond the two slave systems, instead arguing for two separate pools of resources that contribute to both the processing aspects of working memory and the two slave systems. In their study, Shah and Miyake (1996) demonstrated non-significant
correlations between spatial span and reading span measures, significant correlations between spatial span and spatial ability but not language tasks, and significant correlations between reading span tasks and language tasks but not spatial tasks. In addition, a factor analysis yielded a clear separation of spatial and verbal factors. The researchers cited these findings as evidence of separate working memory resources for spatial thinking and language processing. The debate continues.

**Neuroimaging Evidence of Working Memory Subcomponents**

Further evidence in support of separate working memory structures comes from neuroimaging studies of unimpaired participants performing working memory tasks, and studies of patients with neurological damage (Henson, 2001). These studies show the lateralisation of working memory, with the right hemisphere associated with the maintenance of visuospatial material, and the left hemisphere associated with the maintenance of verbal material (Henson, 2001). Specific regions in the left hemisphere that appear to be activated during verbal working memory tasks include the inferior and superior parietal cortex, the inferior frontal cortex (Broca’s area) and the inferior motor cortex (Awh, Jonides, Smith, Schumacher, Koepepe, & Katz, 1996; Henson, 2001; Smith & Jonides, 1997). Similar regions located in the right hemisphere have been found to be activated during visuospatial maintenance tasks, with the addition of the anterior extrastriate occipital cortex, which is often associated with visual imagery (Henson, 2001; Smith, Jonides, & Koepepe, 1996).

The localisation of the central executive has not been so straight forward. It has generally been associated with the frontal lobes, particularly the left and right dorsolateral prefrontal cortex, although specific localisation often depends on the type of manipulation involved in the task (Baddeley, 2003; Henson, 2001). In an extensive review of neuroimaging studies investigating the central executive, Collette et al. (2006) concluded that executive functioning relies on a neural network that involves both the
prefrontal and the parietal areas, and that the central executive should be conceptualised in terms of different interactions between a network of regions, rather than in terms of a specific association between one region and one executive function.

**Criticism of the Model**

While there have been several over the years, the most common criticism within the literature is that working memory model is under-specified (Andrade, 2001). The model fails to define and explain all of the components involved in working memory and the interrelationships between the components adequately (Andrade, 2001). This is particularly evident with the poorly understood central executive, which many researchers argue is not unitary in nature and should be fractionated (Andrade, 2001; Collette & van der Linden, 2002; Henson, 2001). To date, there has not been an executive task identified in the literature that clearly taps only one, distinct, executive process, nor has there been a task identified that clearly distinguishes the central executive from the slave systems (Collette & van der Linden, 2002).

The simplicity of the model is also quite evident in the visuospatial sketchpad, in that the processes and representations that underlie storage and processing within the sketchpad are poorly explained (Pearson, 2001). Many researchers suggest that the sketchpad should also be fractionated, and would benefit from the addition of material specific stores for visual object and visual spatial material (Henson, 2001; Klauer & Zhao, 2004). Furthermore, the authors themselves (Baddeley et al., 2010) admit that “the episodic buffer remains a somewhat shadowy concept” (p. 240). It remains unclear what are the specific functions of the episodic buffer, and how best to measure it (Baddeley, 2012). Finally, while the phonological loop does not receive the same criticisms of under-specificity, the component is plagued by the ongoing controversy of the trace decay versus interference debate (Baddeley, 2012). The debate centres on whether memory traces within verbal short-term memory decay over time (temporal
decay) or interfere with each other. This debate has yet to be satisfactorily settled (Altman & Schunn, 2012).

**Strength of the Model**

In contrast, specificity and simplicity are also seen as key strengths of the working memory model (Andrade, 2001; Baddeley, 2010). The model is simple and provides a theoretical framework that allows for its application to everyday phenomena, and is a parsimonious account of an extremely large body of cognitive, neuropsychological, and developmental data (Andrade, 2001). The model allows for experimental manipulation of individual working memory components and the generation of novel tasks, rather than being restricted to simple correlational designs (Baddeley, 2012; Phillips & Hamilton, 2001).

Support for the importance of the working memory model for complex cognitive tasks comes from studies using complex span tasks to measure working memory (Jarrold & Towse, 2005). Complex span tasks differ from short-term memory tasks in that they simultaneously engage both the processing and storage aspects of working memory (Turner, & Engle, 1989). Performance on complex span measures is associated with performance on a number of complex cognitive tasks including reading (Daneman & Carpenter, 1980; Hitch, Towse, & Hutton, 2001), mathematics (Hitch et. al., 2001), reasoning ability (Kyllonen & Christal, 1990), and general fluid intelligence (Engle, Tuholski, Laughlin, & Conway, 1999). Furthermore, deficits in working memory performance (as measured using complex span tasks) have been closely associated with poorer academic performance in children (Gathercole & Pickering, 2000).

**Working Memory across the Lifespan**

Across the lifespan, several key changes in working memory performance occur. Performance on tasks measuring the central executive, phonological loop, and visuospatial sketchpad shows similar developmental trajectories, with capacity in each
working memory component increasing linearly from age 4 through to adolescence (Gathercole, Pickering, Ambridge, & Wearing, 2004). The interrelationship between the central executive and the two, independent slave systems has been found to be in place in children as young as 6 years, with no significant developmental changes in the relationships evident from this age (Gathercole et al., 2004). A downwards trajectory is then observed across the lifespan beginning in a person’s 20s, with gradual and regular declines in working memory performance occurring in each decade (Park & Payer, 2006). These declines are similar across both verbal and spatial working memory (Park & Payer, 2006).

**Contrasting Working Memory Perspectives**

While the current thesis will focus on Baddeley and Hitch’s multiple component view of working memory (Baddeley, 2000; Baddeley & Hitch, 1974), a brief discussion is provided here to acknowledge contrasting working memory perspectives. Most perspectives do not challenge the working memory concept as a whole but, rather, challenge aspects of Baddeley and Hitch’s model, particularly the central executive and what underpins individual differences in working memory span. Indeed, many models of working memory do not acknowledge the two storage components of working memory, or reject the idea that these two components contribute to cognitive abilities. For example, Cowan’s Embedded Processes model (1999) proposes that working memory consists of long-term memory representations activated by limited-capacity attentional resources. This model rejects the view of separate short-term and long-term memory stores, instead viewing memory as a continuous process roughly equated with long-term memory, with working memory as a subset of long-term memory. Information from long-term memory is brought into working memory or made more readily accessible. Entry into working memory is made by an embedded subset of information being placed in a state of heightened activation, which is time limited and
prone to decay. A further subset of this activated information can be made even more salient by being brought into the focus of attention (which is capacity-limited). This model focuses on the scope of attention as primarily responsible for individual differences in working memory capacity, with greater capacity for attention associated with better working memory capacity. In terms of Baddeley and Hitch’s working memory model, the Embedded Processes model is comparable with the episodic buffer and central executive components of working memory (Baddeley, 2012).

Engle and colleagues (Engle & Kane, 2004; Engle et al., 1999) take a similar, and yet more functional approach, to that of Cowan’s Embedded Processes model (1999). They, too, propose that short-term memory is represented as long-term memory traces active above threshold, rather than domain-specific storage structures. The researchers propose that the primary mechanism that underpins individual differences in working memory capacity is a domain-free construct called executive attention. Engle and colleagues argue that working memory capacity is associated primarily with the ability to control attention in the face of interference or distractions (for a review, see Engle & Kane, 2004). Baddeley (2012) notes that many of the popular, individual differences-based models are largely comparable with his multicomponent model, typically focusing on the central executive, yet accepting of the contributions from separate visual and verbal short-term memory stores.

**Chapter Summary**

This chapter introduced Baddeley and Hitch’s multiple component model of working memory (1974, 2000). As can be seen from the contrasting perspectives, there remain some arguments as to the structure, function, and general nature of working memory (Miyake & Shah, 1999). Nonetheless, while a number of criticisms have been noted, the working memory model proposed by Baddeley and Hitch stands today as the most widely used and referenced working memory model. The next chapter provides a
brief review of the literature investigating sleep architecture, theories on the function of
sleep, measurement of sleep, and sleep disturbance and the relationship between
disturbed sleep and cognition.

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Chapter 2:

Sleep and Sleep Disturbance
Sleep is the rapidly reversible state of reduced awareness and responsiveness to environmental stimuli, often characterised by stereotypical behaviours such as reclined position, closed eyes, reduced motor activity, and reduced metabolism (Carskadon & Dement, 2011). Once thought to be a passive state of unconsciousness, sleep is now recognised as an active process involving both physiological and neurological activity (Dahl & Lewin, 2002; Stanley, 2005). Without sleep, humans experience a number of adverse health and cognitive outcomes, and animals have been known to die. Yet, the exact function of sleep remains highly contested (McEwan, 2006; Rechtschaffen & Bergmann, 2002; VanDongen, Maislin, Mullington, & Dinges, 2003). Several theories have been proposed to explain the key functions of sleep (Maski, Kotagal, & Kothare, 2011). Three of the most popular theoretical frameworks will be discussed below, following a brief description of sleep architecture.

**Adult Sleep Cycles and Architecture**

Normal sleep is a structured process that involves cycling between two, distinct sleep states: non-rapid eye movement (NREM) and rapid eye movement (REM) sleep (Rama, Cho, & Kushida, 2006). A single cycle typically lasts around 90 minutes in adults, with the initial 80 minutes spent in NREM sleep, followed by ~10 minutes in REM sleep (Maski et al., 2011). The cycle is then repeated and thought to occur between 3 to 6 times in a night (Maski et al., 2011). While the exact purpose of alternating between the two sleep stages in every cycle is unknown, irregular cycles and/or absent sleep stages are associated with sleep disorders (Colton & Altevogt, 2006; Zepelin, Siegel, & Tobler, 2005).

NREM sleep in humans was originally subdivided into four stages (stages 1, 2, 3, and 4) as defined by electroencephalogram (EEG) measurement (Carskadon & Derment, 2011; Rama et al., 2006). However, the American Academy of Sleep Medicine recently produced a new classification system where stages 1, 2, and 3/4 have
been replaced with stages N1, N2, and N3 respectively (Iber, Ancoli-Israel, Chesson, & Quan, 2007). Each stage is characterised by unique variations in brain waves, eye movements, and muscle tone (Colton & Altevogt, 2006). N1 sleep is the transitional state from wakefulness into sleep, and is typically the initial stage of the sleep cycle (Colton & Altevogt, 2006). N1 generally makes up 5 to 7% of total sleep, and it is in this stage that sleep is most easily disrupted by external stimuli (Maski et al., 2011). N2 is a deeper sleep stage which increases throughout each cycle eventually constituting between 45 and 55% of total sleep (Rama et al., 2006). N2 is not as easily disrupted by external stimuli as N1, eye movements are rare, and EMG activity remains low to moderate (Colton & Altevogt, 2006; Maski et al., 2011). N3, or slow wave sleep, predominantly occurs in the first third of the night and makes up 15 to 20% of total sleep time (Colton & Altevogt, 2006; Rama et al., 2006). No eye movements are recorded during this stage, and EMG activity is at its lowest when compared to wakefulness and N1 (Rama et al., 2006; Rechtschaffen & Kales, 1968). The arousal threshold to external stimuli is at its highest during this stage, the deepest type of sleep, compared to the earlier NREM stages (Carskadon & Dement, 2011). During each sleep cycle, a person enters briefly into N1, progressing through stages N2 and then N3, before entering REM sleep.

REM sleep is characterised by muscle paralysis, rapid bursts of eye movements similar to those observed when awake, and desynchronised brain wave activity (Carskadon & Dement, 2011). Neuronal activity during this stage is similar to that seen in wakefulness, and the arousal threshold is similar to that in the N1 and N2 stages (Maski et al., 2011). Dreaming occurs most often during REM sleep (although dreams also occur in NREM sleep), with approximately 80% of all vivid dreams reported following awakening from REM sleep (Dement & Kleitman, 1957). REM sleep accounts for 20 to 25% of total sleep time, and begins 1-1.5 hours after the onset of
NREM (Rama et al., 2006). The ratio of NREM to REM sleep in each sleep cycle changes throughout the night (Colton & Altevogt, 2006). Whereas NREM slow wave sleep is prominent in the first third of the night, REM sleep is more prominent in the last third (Rama et al., 2006).

Figure 1 Sleep stages and cycles in adult sleep. Source: Adapted from Luke Mastin at http://www.howsleepworks.com/types_cycles.html

**Developmental Changes in Sleep Patterns**

Distinct changes in sleep cycles occur throughout life (Crabtree & Williams, 2009). The 3 stages of NREM sleep are identifiable after 6 months of age (Jenni & Carskadon, 2005). REM-NREM cycle length increases to adult values throughout early childhood reaching 60 to 90 minutes around the ages of 4 to 5 years (Raju & Radtke, 2012). Around this age, sleep is consolidated into night-time sleep (daytime naps are ceased) and the percentage of total REM sleep reaches adult levels, which then remains stable throughout life (Sheldon, 2014). By adolescence, sleep duration is around that of adults, typically reported as 8.5 hours per night (Sheldon, 2014).
Theories of Sleep Function

Restoration

Restoration theories propose that the central function of sleep is to allow for the restoration or recovery of the body’s physiological, neurological, and/or psychological states (Webb, 2012). The key premise of this viewpoint is that sleep reverses and/or repairs cellular damage that occurs as a result of wakefulness, by promoting certain biochemical and physiological processes (Sheldon, 2014). Body tissue is thought to be restored during NREM and brain tissue during REM sleep (Sheldon, 2014). Indirect evidence to support restoration theory comes from a number of observations including that several hormones (e.g., growth and anabolic hormones) are released following sleep onset and that there is an increased mitosis of lymphocytes and increased rate of bone growth during sleep (Maski et al., 2011). However, a major weakness is that studies providing evidence to support this viewpoint have largely been correlational in design, and it is possible that the processes responsible for restoration are distinct from the function of sleep (Mignot, 2008).

Energy Conservation

According to this view, the main function of sleep is to reduce energy demands (Sheldon, 2014). Sleep restricts activity for large periods of time, and energy expenditure during these periods is at its lowest (Mignot, 2008). During NREM sleep, metabolic rate (e.g., heart rate, respiratory rate, body temperature) is reduced, resulting in decreased energy expenditure (Akerstedt & Nilsson, 2003; Schmidt, 2014). However, while NREM sleep is associated with decreased energy demands, increased energy expenditure is noted during REM sleep, with some cortical areas as active (or more so) than during wakefulness (Schmidt, 2014). Further, the reduction in metabolic rate from quiet wakefulness to sleep is relatively small (approximately 8% to 10%) when considering the basal metabolic expenditure of a human adult, which makes it unlikely
that energy conservation is the primary function of sleep (Sheldon, 2014; Schmidt, 2014).

Learning and Brain Development

The third theoretical framework is based on the observation that higher-level cognitive abilities, such as learning and memory, are readily impacted by sleep deprivation (sleep loss resulting in insufficient sleep) (Sheldon, 2014). Both NREM and REM sleep are thought to facilitate learning and memory through changes in synaptic plasticity (Mignot, 2008). Key support for post-learning synaptic plasticity has stemmed from the observation that sleep duration increases following learning tasks (particularly REM sleep), and sleep deprivation following learning tasks impairs task acquisition (Bennington & Frank, 2003). While this theory has garnered strong support, it remains unclear what type of learning is most affected by sleep, and which sleep state is most important for learning (e.g., REM versus NREM) (Frank & Bennington, 2007). Furthermore, learning and plasticity also occur during wakefulness, which brings into question the necessity of sleep (Bennington & Frank, 2003). If the answer is for sleep-dependent consolidation to occur, then it remains for the relationship between sleep and the intracellular events required for both synaptic plasticity and memory formation to be better understood (Ognjanovski, Maruyama, Lashner, Zochowski, & Aton, 2014).

While the primary function of sleep in humans remains unclear, it is highly likely that sleep has evolved several times throughout evolution to serve different functions, and that at this time no single function stands out across species or age groups, making it difficult to provide a parsimonious explanation as to why we sleep (Rechtschaffen, 1998). What is clear is that sufficient sleep appears necessary for sustaining life and for optimal daytime functioning.
Measurement of Sleep

As research into sleep has increased dramatically over the years, so has awareness of the many sleep disorders and disturbances which impair daytime functioning, and the need for systematic ways in which to measure these sleep problems. Three main techniques used within the research field today are discussed below.

**Polysomnography**

Considered the gold standard in the assessment of sleep architecture, sleep disorders, and respiratory parameters, polysomnography (PSG) works by measuring physiological signals from many different organ systems (including the brain) throughout the night (Togeiro & Smith, 2005). PSG is able to provide a number of measurements including EEG, EMG, EOG, electrocardiogram (electrical activity of the heart), oronasal flow, thoracoabdominal movement, body position, oesophageal pressure, and snoring (Togeiro & Smith, 2005). Despite the wealth of reliable and valid objective data PSG can provide, there are a number of disadvantages when using this method of sleep measurement, particularly within a paediatric population (Griebel & Moyer, 2006). Costs are high (estimated to be approximately $2625 US per participant), and the method is inconvenient (PSG is labour and time-intensive). Further, PSG can be invasive, as it involves overnight sleep studies that are typically run in a laboratory or hospital setting, which require the assistance of a specialist to place electrodes on the required bodily areas (Khatwa, Ramgopal, Singh, Loddenkemper, Zarowski, & Kothare, 2013). PSG in paediatric populations is particularly tricky, especially in children with special needs (e.g., attention deficit hyperactivity disorder, intellectual disability, autism) as children are often noncompliant with the setup of the electrodes, and have difficulty sleeping in a strange environment (Khatwa et al., 2013; though see Bessey, Richards & Corkum, 2013, who showed that typically developing children and children
with attention deficit hyperactivity disorder adjusted similarly to sleeping in a sleep lab). While portable PSG systems have been designed to be used in the home, the risk therein lies in electrodes being displaced during the night resulting in degraded signals. Without an attendant technician, there is no one to replace the displaced electrodes. This reduces the quality of the study (Togeiro & Smith, 2005). A further limitation of paediatric PSG is that there is a lack of normative reference values, making interpretation of abnormal PSG and accurate diagnosis of sleep disorders difficult (Montgomery-Downs, O’Brien, Gulliver, & Gozal, 2006). In light of these limitations, other methods of assessing sleep are becoming increasingly popular, one of which is actigraphy.

**Actigraphy**

Actigraphy is the continuous measurement of body movement in order to determine sleep and wakefulness based on motor activity (Acebo, 2006). Movement is monitored using small, watch-like devices (actigraphs) worn around the wrist or ankle, which detect and record motion and feed the information into software programs (Togeiro & Smith, 2005). The devices can be worn over consecutive days or weeks (a minimum of 5 consecutive nights is recommended in paediatric populations) (Acebo, 1999) and the output recorded generates a number of sleep measures through the use of algorithms, including sleep onset time, total time asleep, sleep efficiency (sleep duration as a percentage of the time spent in bed), number of awakenings, and wake after sleep onset (WASO) (Sadeh, Gruber, & Raviv, 2003). The estimations of sleep and wakefulness are based on the observation that there is decreased movement in humans during sleep as opposed to wakefulness (Ancoli-Israel et al., 2003). While actigraphy does not replace the usefulness of PSG, it provides a more cost effective, less labour intensive and less invasive method of sleep measurement than PSG (Togeiro & Smith, 2005). Further, children are more accepting of this method of assessment, relative to
 PSG sleep studies (Togeiro & Smith, 2005). Correlations, between PSG sleep recordings and actigraphy-based whole-night measures of sleep and sleep efficiency in adults are high (> .80) for non-patient groups (Acebo, 2006). However, actigraphy has been demonstrated to be a poor predictor of sleep quality as reflected by poor estimates of nocturnal awakenings in children, due to its reliance on activity alone to infer sleep and waking (e.g., Montgomery-Downs, Crabtree, & Gozal, 2005; Sitnik, Goodlin-Jones, & Anders, 2008; Spruyt, Gozal, Dayyat, &Molfese, 2011). In a review of paediatric sleep studies validating actigraphy against other sleep measures (primarily polysomnography), Meltzer et al. (2012) noted that out of the 10 studies reporting measures of specificity (wake after sleep onset agreement), more than half reported specificity below 60%. In one study comparing minute-by-minute sleep-wake scorings as measured by videosomnography (video recording of sleep/wake behaviour) and actigraphy in young children (aged 2 to 6 years), Sitnik et al. (2008) demonstrated 94% overall agreement, 97% sensitivity (sleep agreement), and 24% specificity over the course of two consecutive nights. Results from the Sitnik et al. (2008) study showed children on the video recording sitting up in bed and moving, despite the actigraph recording the child as asleep. Actigraphy has also been shown to be a poor predictor of specificity in children with chronic illness (e.g., asthma, juvenile chronic arthritis) relative to typically developing children (Ward, Lentz, Kieckhefer, & Landis, 2011), and may also be unreliable in some special needs populations such as non-medicated children with attention deficit hyperactivity disorder (Waldon et al., 2016). Ward et al. (2011) note that changes in sleep are unlikely to be uniform across paediatric chronic conditions and that the algorithms and thresholds used to score actigraphic parameters need to be customised accordingly.
Sleep questionnaires

Sleep questionnaires are a subjective rating (usually retrospective) of a child’s or adult’s sleep behaviour, that can be used for screening or diagnosis of sleep problems, monitoring treatment effectiveness, epidemiological studies, and clinical research (Togeiro & Smith, 2005). While lacking the objectivity that actigraphy and PSG provide, sleep questionnaires provide a method of assessment which is efficient, inexpensive, and convenient. One of the main strengths of sleep questionnaires is that large samples of children can be easily recruited, relative to polysomnography and actigraphy. Further, unlike the former two measurements, data are easily collected from both clinical and non-clinical populations alike. Thus, given the need to recruit large samples of both clinical and non-clinical groups of children in the current research, we chose to use a children’s sleep questionnaire across all three studies. We chose the Sleep Disturbance Scale for Children (SDSC; Bruni et al., 1996) based on a review investigating the psychometric properties of children’s sleep questionnaires (Spruyt & Gozal, 2011). In the review, Spruyt and Gozal (2011) noted that many of the paediatric questionnaires used in current research lack psychometric properties such as item-analyses, validity, reliability and norms. Spruyt and Gozal (2011) identified only two children’s sleep questionnaires that fulfilled all of the desirable criteria of a sound psychometric tool - the Sleep Disturbance Scale for Children (SDSC; Bruni et al., 1996) and the Sleep Disorders Inventory for Students-Children and Adolescent form (Luginbuehl, 2003). Of the two questionnaires, we chose to use the SDSC based on the extensive number of sleep disorders covered across the six subscales.

Sleep Disturbance Scale for Children

The SDSC is a 26-item, parent-report, sleep questionnaire that assesses sleep-wake patterns and sleep behaviours. Specifically, the questionnaire assesses six subscales: disorders of initiating and maintaining sleep; sleep-disordered breathing
disorders; disorders of arousal; sleep-wake transition disorders; disorders of excessive somnolence (sleepiness); and sleep hyperhydrosis. The questionnaire takes around 10 minutes to complete and is easy to administer, with the six subscales rated on a 5-point Likert scale. The original version was designed for children aged 6 to 15.3 years, and provides normative data based on an Italian sample. Internal consistency was .79 for the control group and .71 for a sleep disordered children’s group, and test-retest reliability was good at .71. The questionnaire is provided free of charge, and has been translated into several languages while maintaining its validity and reliability (Spruyt & Gozal, 2011).

**Defining Sleep Disturbance**

One limitation when reviewing and attempting to generalise the results from children’s sleep studies is the varying definitions of sleep disturbance in children. There are over 80 sleep disorders, each with its own diagnostic criteria, listed in the International Classification of Sleep Disorders-Revised (American Academy of Sleep Medicine, 2001; ICSD). Many research studies have failed to use the diagnostic criteria outlined in the ICSD when defining sleep disturbance in children (Mindell, Kuhn, Lewin, Meltzer, & Sadeh, 2006). This may be due to a number of reasons, particularly a reliance on parental report of children’s sleep habits (Mindell et al., 2006).

**The International Classification of Sleep Disorders – Revised (ICSD)**

The ICSD is the most commonly used classification system for sleep disorders. It categorises sleep disorders into three main types: dyssomnias, parasomnias, and sleep disorders associated with mental, neurological, and other medical disorders. These three ICSD categories are described below.

**Dyssomnias**

The dyssomnias are the primary sleep disorders that generate excessive somnolence and difficulty in initiating and maintaining sleep. Within the ICSD,
Dyssomnias are divided into intrinsic sleep disorders, extrinsic sleep disorders, and circadian rhythm disorders. These categories are based, in part, on pathophysiological mechanisms.

**Dyssomnias (Intrinsic Sleep Disorders)**

Intrinsic dyssomnias are sleep disorders that originate, or are generated, from causes within the body. Common, intrinsic sleep disorders include several types of insomnia and hypersomnia, narcolepsy, periodic limb movement disorder, restless leg syndrome, and obstructive sleep apnoea syndrome. Obstructive sleep apnoea is characterised by complete or partial obstruction of the upper airway that occurs intermittently throughout the night resulting in oxygen desaturation (episodic hypoxia) and increases in carbon dioxide (hypercarbia) (Blunden, Lushington, Kennedy, Martin, & Dawson, 2000; Saunamaki & Jehkonen, 2007). The hypoxia and hypercarbia result in increased respiratory effort and sleep fragmentation, as individuals wake up to breathe (Beebe & Gozal, 2002; Blunden et al., 2000).

**Dyssomnias (extrinsic sleep disorders)**

The extrinsic dyssomnias are sleep disorders that originate, or are generated, from external factors outside of the body. The removal of the external factors producing and maintaining the sleep disorder leads to its resolution. Extrinsic dyssomnias include environmental sleep disorder, altitude insomnia, drug/alcohol-dependent sleep disorders, and food allergy insomnia. One extrinsic dyssomnia highly relevant to the current thesis is inadequate sleep hygiene, as it is significantly associated with how well children sleep (Mindell, Meltzer, Carskadon, & Chervin, 2004). Inadequate sleep hygiene is due to a number of different behavioural activities performed during a person’s daily routine that disrupt the quality and quantity of sleep. These activities include the use of electronic devices before bed, caffeine intake (e.g., energy drinks and
cola), inappropriate naps, inconsistent wake and sleep times, and a lack of consistent bedtime routines (Mindell et al., 2004).

**Dyssomnias (Circadian-Rhythm Sleep Disorders)**

The circadian rhythm disorders share a common, underlying, chronophysiological basis. A misalignment occurs between an individual’s actual sleeping period and the ability to sleep when sleep is desired, needed, or expected (e.g., due to societal norms). This results in sleep and wake periods occurring at inappropriate times. Circadian rhythm sleep disorders include time zone change disorder, shift work sleep disorder, and irregular sleep-wake pattern. Circadian rhythm sleep disorders are more commonly seen in children with developmental disorders (e.g., autism) than in typically developing children (Jan & Freeman, 2004).

**Parasomnias**

Parasomnias are not considered abnormalities of the processes responsible for the sleep and wake states per se, but are disorders of arousal, partial arousal, and sleep-stage transition that occur due to undesirable phenomena that intrude on the sleep process, but do not cause a primary complaint of insomnia or excessive somnolence. The ICSD further divides the parasomnias into four categories: arousal disorders (e.g., sleep walking and sleep terrors), sleep-wake transition disorders (e.g., rhythmic movement disorder and sleep talking), parasomnias usually associated with REM sleep (e.g., nightmares and sleep paralysis), and other parasomnias (e.g., sleep enuresis, sleep bruxism, and primary snoring).

**Other sleep disorders**

Sleep disorders associated with mental, neurological, and other medical disorders are not primary sleep disorders, but are manifestations of excessive daytime sleepiness or insomnia associated with a psychiatric or medical illness. For example, mood disorders and anxiety disorders are frequently seen in children presenting to
doctors with complaints of sleep disturbance. Other medical illnesses such as chronic obstructive pulmonary disease, sleep-related epilepsy, and sleep-related asthma are also listed in this category as they, too, are characterised by features that occur during sleep or cause sleep disruption.

**Prevalence Estimates of Sleep Problems in Children**

Approximately one third of all primary school-aged children are estimated to have significant sleep complaints (Mindell & Owens, 2009). Specifically, obstructive sleep apnoea affects approximately 1 to 5% of children (Carter, Hathaway, & Lettieri, 2014), while other dyssomnias, such as restless leg syndrome, narcolepsy, insomnia, and periodic limb movement disorder affect approximately 2% (Moore, Alison, & Rosen, 2006). Parasomnias are more common in children than dyssomnias, with the prevalence of sleepwalking disorder estimated at 5 to 17% (Carter et al., 2014; Goodwin et al., 2004), night terrors at 1 to 6% (Carter et al., 2014), enuresis at 3 to 10% (Laberge et al., 2000), sleep talking at 5 to 10%, and primary snoring at 5 to 12% (Goodwin et al., 2004; Lumeng & Chervin, 2008). Moreover, there are a number of cases of disturbed sleep where no specific diagnosis has been given but, nonetheless, the perceived or actual variations in sleep during the night still result in impaired daytime functioning (Berger et al., 2005; American Academy of Sleep Medicine, 1990). There are also much higher rates of sleep problems in certain populations of children such as those from low socio-economic (SES) backgrounds, or those with medical, developmental, or psychological disorders (Buckhalt, El-Sheik, & Keller, 2007; Stores, 2007). Indeed, the two clinical populations of children included in the current research have been found to have unusually high prevalence estimates of sleep problems. For example, the risk of sleep problems in children born preterm is over twice that of children born to term (Rosen et al., 2003). Further, prevalence of sleep problems in children with neurological conditions such as autism has been estimated to be as high as 75 to 80% (Jan et al.,
2008). Given the negative effects of poor sleep on a child’s health and wellbeing, the above prevalence estimates are very concerning.

**The Impact of Sleep Problems**

The Deloitte Access Economics paper (Sleep Health Foundation, 2011) estimated the direct cost of sleep disorders (as defined by insomnia, obstructive sleep apnoea, and restless leg syndrome) in adults on the Australian health care system to be over AUS$818 million, while the indirect cost on the economy as a whole was estimated to be around 4.3 billion dollars. The report found that poor sleep in adults was associated with major health costs such as workplace absenteeism, increased motor vehicle and workplace accidents, lower quality of life, depression, and diseases such as diabetes, hypertension, coronary heart disease, and stroke. Although only briefly mentioned in the report, the impact of sleep problems in children is also far reaching. Sleep problems impact upon a child’s physical, emotional, social, and cognitive functioning, as well as exacerbating existing medical, psychiatric, developmental, and psychosocial problems, and creating additional stress, fatigue, and burden for the parent/caregiver (Mindell & Owens, 2009).

**Chapter Summary**

As can be seen, sleep problems in children are highly prevalent, particularly in children from low SES backgrounds, or with medical, developmental, or psychological disorders (Buckhalt, et al., 2007; Stores, 2007). Importantly, past research has demonstrated that sleep problems have a significant impact upon children’s cognitive functioning. Of interest in the current research is the impact of sleep problems on children’s working memory, which will be explored, in detail, in the following chapter.
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Chapter 3:

Sleep and Working Memory
This chapter addresses the relationship between sleep and working memory. It begins with a brief examination of research on sleep and cognition in children and adults. The focus then shifts to research investigating working memory and sleep, followed by possible mechanisms by which sleep may impact upon working memory, and cognition as a whole.

**Cognition and Sleep**

**Cognition and Sleep in Adults**

As noted by Beebe (2011), the extremely well-developed literature on sleep and cognition in adults provides a logical platform from which to begin researching the less prominent area of sleep and cognition in children. Much of the evidence demonstrating the impact of sleep on cognition in adults has come from investigations into sleep deprivation, and from the study of adults with obstructive sleep apnoea. Findings from these research fields have been, largely, in agreement, in that sleep problems in adults have deleterious effects on cognition, particularly attention/vigilance, working memory, and executive functions (Durmer & Dinges, 2005; Lim & Dinges, 2010; Olaithe & Bucks, 2013; Van Dongen et al., 2003; Wallace & Bucks, 2013). While the above results cannot readily be extrapolated to children, due to noted developmental changes in sleep architecture, they strongly suggest that poor sleep may also adversely affect children’s cognition.

**Cognition and Sleep in Children**

Unlike research into sleep and cognition in adults, which stems back over a century, the study of sleep and cognition in children is relatively new, spanning the last two decades (Durmer & Dinges, 2005). The paucity of studies investigating sleep and cognition in children, compared to adults, is most likely because it is easier to study sleep in adults. There are a number of methodological issues that arise when studying children’s sleep that do not exist for adults. For example, for ethical reasons, most
parents would be reluctant to allow a researcher to subject their child to one or two nights of total sleep deprivation. Similarly, most parents would be reluctant to leave their child in a laboratory setting overnight with strangers, and many children would not be able flexibly to adapt to staying in an unfamiliar setting overnight (Beebe, 2011). Similarly, children’s sleep is subject to external factors beyond their control, which can also make investigating associations between sleep and cognition difficult (e.g., parent work schedules, hobbies and activities) (Colton & Altevogt, 2006). As a result, there is still much to be learned about the impact of sleep problems upon children’s cognitive functioning.

Results from the few experimental studies investigating sleep and cognition in school-aged children have been somewhat inconsistent. No experimental study investigating sleep and cognition in primary school-aged children (e.g., 6 to 12 years) has included a night of total sleep deprivation, and many of the sleep restriction studies (studies that manipulate the duration of sleep) have been limited by small sample sizes. Results from studies experimentally reducing the duration of school-aged children’s sleep have shown some evidence of negative effects on attention (Vriend, et al., 2013; Fallone, Acebo, Arnedt, Seifer, & Carskadon, 2001), academic achievement (Fallone, Acebo, Seifer, & Carskadon, 2005), short-term memory and reaction time (Sadeh et al., 2003, Vriend et al., 2013), and working memory (Vriend et al., 2013).

Most studies investigating sleep in school-aged children have been correlational in design. Much like the experimental studies, results from correlational studies investigating the association between sleep and cognition in otherwise typically developing children have been somewhat inconsistent. This lack of consistency may relate to differences in research design, in that outcome and sleep measures vary widely across studies, making it difficult to generalise results. That being said, there is some agreement within the children’s sleep literature that poor sleep quality and/or duration
is associated with poor academic outcomes, decreased vigilance, inattention, slowed processing speed, and executive functioning (Astill, Van der Heijden, Van IJzendoorn, & Van Someren, 2012; Beebe, 2011; Dewald, Meijer, Oort, Kerkhof, & Bogels, 2009; Buckhalt, El-sheikh, & Keller, 2007). Thus, it seems that sleep may be associated with particular aspects of children’s cognition and not others. Of specific interest to the current research is the impact of sleep on children’s working memory. While the adult literature suggests that poor sleep is associated with decreased working memory performance (e.g., Beebe, Groesz, Wells, Nichols, & McGee, 2003; Durmer & Dinges, 2005; Olaithe & Bucks, 2013), the children’s literature is less clear. The next section of this thesis reviews the findings from past research investigating the relationship between sleep and working memory in school-aged children.

Sleep and Working Memory

Sleep and Working Memory in Typically Developing Children

Only two sleep restriction studies (Sadeh et al., 2003; Vriend et al., 2013) have included measures of working memory performance, and the results were contradictory. Sadeh and colleagues (2003) experimentally manipulated 9- to 12-year-olds’ (n = 77) sleep and measured the impact on their neurobehavioural functioning. Participants were assigned to one of two groups that required the participant either to restrict or extend their sleep by one hour for three consecutive nights while their sleep was monitored by actigraphy. Participants were tested on cognitive measures before and after the experimental manipulation. Based on the success of their restriction or extension of sleep, participants were then grouped into three groups; the no change group (with a maximum of 30 minutes sleep restriction or sleep extension), and the extension (>30 minutes extended sleep) and restriction groups (>30 minutes restricted sleep). Extension of sleep led to improved reaction time (as measured by the continuous performance test) and attention (as measured by a forwards digit span task), when compared with sleep
restriction or no change. In contrast, the sleep restriction and no change groups’ performance on a simple reaction time task deteriorated significantly from their baseline performances when compared to the sleep extension group. Nonetheless, there were no effects on digit span backwards (a measure of working memory) for any group.

In a similar, experimental study, Vriend and colleagues (2013) split children aged 8 to 12 years into two groups, with one group increasing their sleep by one hour and one group decreasing their sleep by one hour. After one week of the experimental manipulation, performance was measured on a number of cognitive tasks, including working memory (digit span backwards task). Following this, the sleep manipulation for each group was reversed and performance was again measured after one week. The results revealed decreased working memory performance in the short- compared to the long-sleep condition. We argue, based on the design of the two studies, that the results from the Vriend et al. (2013) study are a more valid representation of the true relationship between sleep and working memory than results from the Sadeh et al. (2003) study. A strength of the experimental design used by Vriend et al. (2013) was that both groups experienced the short and long-sleep conditions and, as such, the participants acted as their own control group. This reduced the amount of error variance associated with individual differences within the study. In contrast, Sadeh et al. (2003) compared performance across three independent samples of children (e.g., the control, sleep extension, and sleep restriction groups), suggesting a much larger amount of error variance was included in the outcome scores relative to the Vriend et al. (2013) study. Further, assignment to sleep groups in the Sadeh et al. (2003) study was based on the success of the sleep manipulation, rather than random assignment, which may also have affected results by introducing confounding factors associated with children’s adherence to the manipulation of sleep (e.g., environmental or behavioural factors).
Much like sleep restriction studies, treatment studies investigating cognitive performance in children undergoing adenotonsillectomy in order to treat sleep disordered breathing provide the opportunity to show support for a causal relationship between children’s sleep and working memory performance. Performance is measured before treatment, and then several months after treatment following improvement of the sleep disordered breathing. Much like the two sleep restriction studies mentioned above, results from the only two treatment studies examining children’s working memory performance are contradictory (Giordani et al., 2012; Kohler, Lushington, van den Heuvel, Martin, Pamula, & Kennedy, 2009). Kohler et al. (2009) investigated sleep problems and working memory performance in children awaiting adenotonsillectomy. The researchers compared both verbal and nonverbal working memory performance in 44 children with sleep disordered breathing and 48 healthy children, aged 3 to 12 years, before and 6 months after treatment. Pre-treatment, children with sleep disordered breathing showed poorer performance on both verbal and nonverbal working memory tasks relative to the control group. However, the researchers were unable to provide support for a causal relationship between sleep problems and working memory performance, as no improvements in verbal or spatial working memory performance 6 months following treatment were observed. The researchers did note that 6 months post-operation may not have been enough time in which to see improvement.

In contrast, Giordani et al. (2012) allowed for 12 months post-operation before retesting children’s cognitive performance and found significant improvements on working memory measures. In an earlier study, Giordani et al. (2008) investigated working memory performance (as measured by subtests from the Children’s Memory Scale; Cohen 1997) in children (aged 5 to 12 years) with varying degrees of sleep disordered breathing awaiting adenotonsillectomy. The researchers found that, when compared to the control group (n = 27), the mild sleep disordered breathing group
(\(n = 27\)) performed significantly worse on the working memory subtests while the severe sleep disordered breathing group (\(n = 40\)) did not. Children’s cognitive performance was then assessed for the second time, one year post-operation (Giordani et al., 2012). The investigators found that children in both the mild and severe sleep disordered breathing groups had improved in terms of performance on the working memory measures (and sleep-related PSG measures), supporting a causal link between sleep problems and working memory deficits. Thus, it appears that Kohler et al. (2009) may have been correct in their conclusion that 6 months post-operation is too short a period of time to detect working memory improvements following adenotonsillectomy, which is consistent with research suggesting cognitive deficits associated with sleep breathing disorders are quite persistent (e.g., Beebe & Gozal, 2002). Nonetheless, more treatment studies are needed to confirm the 12-month timeframe.

Congruent with the above experimental studies, findings from correlational studies investigating sleep and working memory in school-aged children have also been mixed. Recently, Astill et al. (2012) conducted a meta-analysis on studies examining sleep and cognition in healthy children aged 5 to 12 years. The researchers broke cognition down into seven subdomains, one of which was executive functions which encompassed inhibitory control, cognitive flexibility, and working memory. The researchers found that curtailment of sleep duration was associated with compromised executive functioning, while no association was found between sleep efficiency and executive functioning. These results suggest that executive functioning and, by association, working memory performance, are more sensitive to sleep duration than sleep efficiency. However, as working memory was not measured as a separate construct, it is difficult to discern whether working memory was uniquely associated with sleep duration. Importantly, several studies have found evidence of a direct relationship between sleep and working memory in healthy, typically developing
children (e.g., Buckhalt et al., 2007; Steenari, Vuontela, Paavonen, Carlson, Fjallberg, & Aronen, 2003). Similarly, typically developing children with diagnosed sleep problems have been found to perform more poorly on measures of working memory when compared to children with no diagnosed sleep problems (e.g., Biggs et al., 2011; Bourke et al., 2011, Halbower et al., 2006).

Conversely, several studies have failed to find a relationship between sleep and working memory in typically developing school-aged children (Archbold et al., 2004; Beebe et al, 2004; Biggs et al., 2011; Calhoun et al., 2009; Vriend, Davidson, Corkum, Rusak, McLaughlin, &Chambers, 2012). For example, Archbold et al. (2004) found that children with mild sleep disordered breathing awaiting adenotonsillectomy (n = 12; aged 8.0 to 11.9) did not differ significantly from normative data on the working memory subtests from the CMS, although the researchers noted that the small sample size was a severe limitation to their study. Vriend et al. (2012) measured the sleep of healthy 8- to 12-year-olds (n = 28) using actigraphy for one week, and then tested their verbal and nonverbal working memory using the digit span backwards task from the WISC-IV and the finger window task respectively. They found no association between sleep and working memory. However, a limitation noted in their study, besides the small sample size, was the reduced variability in sleep parameters and cognitive performance due to study inclusion criteria (e.g., no sleep problems, and no learning, behaviour, or mental health problems). The researchers proposed that greater variability in the sample may have allowed for the detection of a relationship between sleep and working memory.

**Sleep and Working Memory in Children with Neurological Conditions and Children Born Very Preterm**

Two populations of children who provide an opportunity to investigate greater variability in working memory performance and sleep disturbance are children with congenital and/or acquired neurological conditions, and/or children born very preterm.
Given these two populations of children have been found to be at increased risk of sleep problems relative to typically developing/born to term children (e.g., Beebe, 2012; Dorris, Scott, Zuberi, Gibson, & Espie, 2008; Kothare & Kotagal, 2011; Rosen et al., 2003), including these children in our investigations provides the best chance to observe a relationship between sleep and working memory, and to systematically assess the potential mechanisms underlying any relationship. This in turn will help to resolve some of the inconsistencies in the literature, and potentially result in clinical implications that assist in future interventions in children with neurological conditions and children born very preterm. Nevertheless, surprisingly few studies have investigated the relationship between sleep and cognition in these children, and even fewer have explored sleep and working memory. Despite numerous studies revealing that children with a range of neurological conditions are at increased risk of reduced working memory performance (e.g., Conklin, Salorio, & Slomine, 2008; Jenks, de Moor, & van Lieshout, 2009; Longo, Kerr, & Smith, 2013), only four studies have investigated the relationship between sleep and working memory performance in this population of children. Of the four studies, two investigated the relationship in school-aged children with ADHD (Sawyer et al., 2009; Zambrano-Sanchez, Martinez-Cortes, Dehesa-Moreno, Rio-Carlos, & Poblano, 2013), one in children aged 1 to 15 years with autism (Mayes & Calhoun, 2009), and one in children aged 6 to 13 with epilepsy (Holley et al., 2013). Both studies investigating the relationship in children with ADHD, found that sleep problems were associated with working memory deficits. Conversely, Mayes and Calhoun (2009) failed to find an association in children with autism, as did Holley et al. (2013) in children with epilepsy. Clearly, the research is less than conclusive and appears to be limited to a small number of specific, diagnostic categories.

No study, to date, has investigated the relationship between sleep disturbance and working memory in children born very preterm. Results from the only study to have
investigated sleep disturbance and cognitive functioning more generally in children born very preterm (Hagmann von Arx et al., 2014), suggest that disturbed sleep may very well play a role in the cognitive functioning of very preterm children. Hagmann von Arx (2014) found significant associations between disturbed sleep and cognitive functions (intelligence, visuospatial memory, arithmetic, and selective attention) in children born very preterm, whereas no associations were found in children born to term.

What can be seen from the few studies investigating sleep and cognition in children with neurological conditions and/or children born very preterm, is that these two populations of children appear to be cognitively vulnerable to the impact of sleep problems to which they are at risk, and that investigating the relationship between sleep and working memory may potentially help to explain their cognitive difficulties.

**Criticisms of the Children’s Sleep and Working Memory Literature**

There are several major limitations to the existing research, the most critical being the large variability in the tasks used to assess working memory performance. A review of the literature reveals that some studies have used sequencing and digit span tasks (e.g., Giordani et al., 2008; Kohler et al., 2009), some have used n-back tasks (e.g., Biggs et al., 2011; Steenari et al., 2003), some have used complex span tasks (e.g., Halbower et al., 2006), and others have used parent-report questionnaires (e.g., Bourke et al., 2011, Biggs et al., 2011). The lack of consistency in the measurement of working memory performance makes it extremely difficult to generalise results across studies.

Moreover, many models propose a distinction between verbal and nonverbal working memory, and the resources that cognitive tasks associated with each use (e.g., Shah & Miyake, 1996), but very few children’s sleep studies have included measures of both verbal and nonverbal working memory. Indeed, of those that have, several have found differences between the two modalities (e.g., Lau et al., 2015; Steenari et al.,...
2003). Of particular relevance to the current thesis is the Lau et al. (2015) study, which found that children with obstructive sleep apnoea, compared with controls, performed more poorly on a verbal working memory task, whereas no difference in performance between the two groups was noted on the tasks measuring visuospatial working memory performance. Without including measures of both verbal and nonverbal tasks, it is difficult to know whether sleep disturbance may relate more closely to a specific modality of working memory. To take this line of inquiry one step further, sleep may in fact relate more closely to a specific component of working memory, or indeed, relate more closely to a specific component of working memory applied to one modality and not the other.

A further limitation of the measurement of working memory within children’s sleep research is the failure to include independent measures of the three subcomponents of working memory – storage capacity, processing speed, and the central executive. To the best of the current researcher’s knowledge, no sleep study with children has broken down working memory into its three subcomponents. While one study purported to measure the impact of obstructive sleep apnoea upon the central executive using an n-back task (Lau et al., 2015), the study failed to control for the unique variance contributed to working memory performance by storage capacity and processing speed, despite including an independent measure of storage capacity. Given that past research has demonstrated the separability of the three working memory components (e.g., Bayliss et al., 2003; Jarrold et al., 2014), it is paramount that one accounts for the variance contributed by the remaining two components (e.g., processing and storage) when claiming to be measuring a specific working memory component (e.g., the central executive). For example, studies have shown that both processing speed and storage capacity contribute unique variance to working memory performance, and that the residual variance thought to represent the executive
coordination of the processing and storage components is associated with fluid intelligence (e.g., Bayliss et al., 2003; Jarrold et al., 2014). Thus, in order to clearly understand exactly how and where working memory performance is breaking down, so as to be able to tailor interventions to target the appropriate abilities, the impact of sleep upon all three working memory components in children needs to be investigated.

There are a number of further limitations in the sleep and working memory literature to date, such as small sample sizes, a lack of control groups, and a failure to control for potential confounding variables, particularly age and SES (e.g., Sadeh et al., 2003; Vriend et al., 2013), which have been found both to impact upon working memory performance and to influence the risk of poor sleep (Buckhalt et al., 2007; Gathercole, Pickering, Ambridge, & Wearing, 2004). One central limitation to the current literature yet to be discussed is the lack of investigation into the potential mechanisms by which sleep impacts upon children’s working memory (or cognition in general). The following section of this chapter focusses on proposed mechanisms by which sleep impacts upon children’s cognition.

The Mechanisms by which Sleep Impacts upon Children’s Cognition

When investigating the relationship between sleep and cognition in children, very few studies have included investigations into the possible mechanisms underlying the relationship. As a result, the mechanisms by which sleep impacts upon children’s working memory performance remain unclear. There are two main classes of theories that will be discussed in this chapter. The first class of theories contains variants of the vigilance hypothesis, which proposes that sleep-related decrements in cognitive performance are simply due to decreased attention and alertness (e.g., Dorian, Rogers, & Dinges, 2005; Durmer & Dinges, 2005; Williams, Lubin, & Goodnow, 1959). The second class of theories is based on the sleep-based neuropsychological perspective that postulates that poor sleep has a selective effect upon specific brain structures and
functions that, in turn, impairs cognition (e.g., Beebe & Gozal, 2002; Harrison & Horne, 1998, 2000).

**The Vigilance Hypothesis**

The vigilance hypothesis is based on Borbely’s (1982) two-process model of sleep regulation (Alhola & Polo-Kantola, 2007). The two-process model proposes that a sleep homeostatic process (process S) and a circadian process (process C) interact to generate the timing and structure of sleep, and that this interaction also accounts for fluctuations in levels of attention and vigilance (Borbely & Acherman, 1999). Process S represents the drive for sleep that is thought to rise during wakefulness and decline during sleep (Borbely & Acherman, 2007). When the drive increases above a certain threshold, sleep is triggered, and when it decreases beyond a second threshold, wakefulness is triggered (Durmer & Dinges, 2005). The longer a person stays awake, the more the biological need to sleep increases. This increased sleep propensity is typically operationalised as daytime sleepiness (Goel, Rao, Durmer, & Dinges, 2009).

The vigilance hypothesis rests on the premise that alertness and attention are not only fundamental for the performance of cognitive tasks, but are also the most consistently and dramatically impacted by insufficient sleep (Killgore, 2010). The vigilance hypothesis is based on evidence from adult sleep deprivation studies, which suggests that attentional lapses, slowed responses, and wake-state instability associated with sleep deprivation or insufficient sleep lead to a reduction in cognitive performance (on lapse hypothesis see Dorian et al., 2005; Williams et al., 1959; on state instability hypothesis see Durmer & Dinges, 2005).

**Criticisms of the Vigilance Hypothesis**

The main criticism of the vigilance hypothesis is that the effects of daytime sleepiness are readily reversible, which makes it difficult for the hypothesis to account for the more persistent cognitive deficits seen in moderate to severe cases of sleep.
disordered breathing (Beebe & Gozal, 2002). For example, while interventions such as caffeine and naps have been found to counteract the effects of sleep loss and daytime sleepiness resulting in rapid improvements in performance on tasks measuring arousal and attention (Dorrian et al., 2005), many of the cognitive deficits associated with obstructive sleep apnoea (particularly executive functions) remain resistant to treatment (see Marcus et al., 2013). The pervasiveness of the cognitive deficits associated with obstructive sleep apnoea suggests these deficits are not solely due to inattention or reduced alertness associated with simple sleepiness. Thus, while the vigilance hypothesis may explain reduced arousal which impacts on some cognitive tasks, it is unlikely that poor arousal is the primary or sole mechanism by which sleep impacts cognitive performance in children.

The Sleep-Based Neuropsychological Perspective

The sleep-based neuropsychological perspective posits that sleep loss adversely affects certain cerebral structures resulting in impaired cognitive performance (Alhola & Polo-Kantola, 2007). One of the first proponents of this perspective, Harrison and Horne (2000), argue that insufficient sleep impacts primarily upon cognitive performance associated with activity in the prefrontal cortex. Accordingly, tasks measuring higher-order cognitive abilities (e.g., working memory, abstract reasoning, and cognitive flexibility) are posited to be most vulnerable to the effects of reduced sleep relative to more basic cognitive abilities. The sleep-based neuropsychological perspective postulates that sleep-related deficits in higher-order cognitive performance are not simply a result of a breakdown in attention or alertness, but rather a result of the tasks themselves placing demands on a vulnerable region of the brain – the prefrontal cortex (Harrison and Horne, 2000). Evidence from adult neuroimaging reveals the prefrontal cortex to be among the first cerebral regions affected by sleep deprivation (e.g., Muzur et al., 2002; Thomas et al., 2000). Neuroimaging studies have shown that
sleep deprivation is associated with significant declines in the glucose metabolism of several regions within the prefrontal cortex associated with higher-order cognition, including the dorsolateral, ventrolateral, and medial prefrontal cortices (Thomas et al., 2000; Wu et al., 2006).

**Beebe and Gozal’s Model (2002)**

In a comprehensive review, Beebe and Gozal (2002) proposed a theoretical framework based on the sleep-based neuropsychological perspective, linking specific aspects of obstructive sleep apnoea (i.e., sleep disruption, intermittent blood gas abnormalities, for example, hypoxia) and executive dysfunction via insult to the prefrontal cortex. This is one of the most widely accepted explanations of the mechanisms underlying the cognitive deficits in children with sleep disordered breathing (Biggs, Nixon, & Horne, 2014). In this model, arousal and gas exchange abnormalities (due to intermittent hypoxia and hypercarbia) lead to disruption of the restorative features of sleep and/or disrupt cellular homeostasis in particular brain regions. Beebe and Gozal (2002) argue that the adverse cellular and biochemical events triggered by obstructive sleep apnoea lead to dysfunction in the prefrontal cortex and, consequently, executive dysfunction. The model was updated in 2005 (see Figure 3.1), to account for additional factors not necessarily related to obstructive sleep apnoea that directly affect neurobehavioural functioning or act as potential moderators. For example, the model includes factors such as inherited strengths and weaknesses, socioeconomic variables, and task specific demands, all of which that are known to influence cognitive performance.
Criticisms of the Model

The ‘conundrum’ for this model, as Biggs and colleagues (2014) note, is the focus on the specific aspects of obstructive sleep apnoea to the exclusion of the consequences of other types of sleep disturbance. As Biggs et al. (2014) point out, research suggests that primary snoring without hypoxia or increased arousals may also be sufficient to result in cognitive deficits (for a review, see Blunden & Beebe, 2006; Biggs et al., 2014). Indeed, history of chronic snoring has been found to be a better predictor of cognitive deficits in children than other measures of sleep breathing disorders, including polysomnography (Emancipator et al., 2006). Moreover, there is evidence that sleep disturbance in children with non-respiratory sleep disorders, and restricted sleep in otherwise healthy children, also result in cognitive deficits (Randazzo et al., 1998; Steenari et al., 2003; Vriend et al., 2013). Biggs and colleagues (2014) question whether current recording techniques and definitions are sensitive enough to detect hypoxia and/or sleep disruption associated with sleep problems other than sleep breathing disorders (e.g., primary snoring, sleep deprivation). In a review, Beebe (2006)
notes that sleep deprivation and intermittent hypoxia may have parallel or common mechanistic pathways. Animal research has shown that experimental sleep deprivation results in oxidative stress, inflammatory processes, and inhibition of hippocampal long term potentiation and neurogenesis, all of which are also thought to be key mechanisms by which intermittent hypoxia impacts on neurobehavioural functioning. Clearly, this research needs to be transferred to human studies in order to further our understanding of the mechanisms underlying the relationship between sleep and children’s cognitive functioning.

**Aims and Organisation of this Thesis**

As can be seen from the literature review presented in this chapter, the evidence to support an association between sleep and working memory performance is inconsistent. The generalisability of results across studies is limited due to the inconsistency in defining and operationalising working memory. Further, many studies have not approached working memory from a theoretical perspective and, as such, have failed to take into consideration the impact of sleep upon the multiple components of working memory. Nor have many studies considered the mechanisms underlying the relationship between sleep and cognition in children. Given these issues, there were two general aims of this thesis. The first was to investigate sleep and working memory in school-aged children. This was achieved through a series of studies that examined sleep and working memory in three different child samples: typically developing children; children with neurological conditions; and, more specifically, children born very preterm. As mentioned previously, investigating sleep and working memory in these three populations of children allows for a more thorough examination of the relationship because of the greater variability in cognitive and sleep parameters. The second aim of the thesis was to investigate the mechanisms by which sleep impacts upon cognition, by specifically testing the two, key, mechanistic theories: the vigilance hypothesis and the
sleep-based neuropsychological perspective. These aims were addressed across a series of studies.

The study reported in Chapter 4 investigated the relationship between sleep and working memory in typically developing school-aged children. This study employed multiple working memory measures in order to assess children’s performance on the different components (e.g., processing speed and storage capacity) and modalities (verbal and nonverbal) of working memory, in order to observe any unique relationships between sleep and working memory. The inclusion of independent measures of the individual working memory components allowed for the removal of any variance associated with individual differences in processing speed and storage capacity, in order to investigate a possible relationship between sleep and the central executive and, consequently, assess the sleep-based neuropsychological perspective. Several measures of sleep were included to investigate a wide range of sleep problems common in children including snoring, disorders of arousal, and sleep quality in general. A measure of daytime sleepiness was included in order to test the vigilance hypothesis.

The study in Chapter 5 investigated the relationship between sleep and working memory in children with neurological conditions, a population known to have both increased sleep disturbance and reduced working memory, relative to typically developing children. The methodology was consistent with the previous study in that verbal and nonverbal measures of working memory, in addition to specific measures of processing speed and storage capacity, were used to assess performance in children. The sleep measures, again, included measures of snoring, daytime sleepiness, and sleep quality.

The third and final study, in Chapter 6, focused specifically on the association between verbal working memory performance and sleep in children born very preterm. Recent research (see Hagmann von Arx et al., 2014) showed that poor sleep is
associated with a number of cognitive difficulties (though working memory was not assessed) in children born very preterm. Given children born very preterm are also at increased risk of working memory difficulties, we felt this population of children provided an excellent opportunity further to explore the sleep and working memory relationship and potential underlying mechanisms. Further, it was hoped that the clinical implications from our findings might aid in the early identification and treatment of children born very preterm who are at risk of working memory difficulties. Again, measures included verbal working memory, processing speed, storage capacity, snoring, daytime sleepiness, and sleep quality. We expected to find support for the sleep-based neuropsychological perspective, in that sleep would be associated with the executive component of working memory. As such, a measure of abstract reasoning was included to investigate the impact of sleep upon executive functioning directly, with performance on the executive measure compared between typically developing children and children born very preterm. The findings of this thesis and the implications for the current mechanistic models of sleep and cognition are discussed in Chapter 7.

References


Chapter 4:

Sleep and Working Memory in Typically Developing School-Aged Children

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Abstract

The current study examined the relationship between sleep and working memory performance in typically developing, school-aged children. Parent-reported measures of sleep quality, disorders of arousal, and daytime sleepiness were collected on 78 healthy children aged 7- to 11 years old, who attended the University of Western Australia’s Project K.I.D.S. (Kid’s Intellectual Development Study) during July 2011 through to July 2012. Children completed verbal and spatial working memory tasks, as well as measures of storage capacity, and processing speed. Results revealed no significant associations between any of the sleep and cognitive measures. While our findings are consistent with Sadeh et al. (2003) and Vriend et al. (2012), one limitation which may have influenced the current results was the lack of variability in participants’ scores within the sleep parameters, with very few parent’s reporting significant sleep problems in their children.
Working memory is a multicomponent system which temporarily stores and manipulates a limited amount of information in order to perform higher order cognitive tasks (Baddeley, 1992). According to the most prominent model (Baddeley & Hitch, 1974; Baddeley, 2000), working memory incorporates a central executive, two slave systems responsible for the temporary storage of verbal (phonological loop) and spatial (visuospatial sketchpad) information, and an episodic buffer which binds information between the three working memory components and long term memory (Baddeley, Allen, & Hitch, 2011). This multicomponent system is thought to play a critical role in the acquisition of new skills and knowledge, and to be fundamental for learning, reasoning, and language acquisition (Biggs et al., 2011; Baddeley, 1992). Working memory performance varies widely among children, with poor working memory performance often associated with learning difficulties and poor academic outcomes (Alloway, Gathercole, Kirkwood, & Elliot, 2009). Despite the importance of working memory in a developmental context, relatively few studies have investigated the mechanisms that underlie these individual differences in children. One possible factor that has become the focus of recent research is sleep.

The adult literature indicates that sleep plays an important role in the functioning of working memory, with poorer sleep quality associated with impaired working memory performance (Lim & Dinges, 2010; Olaithe & Bucks, 2013). Further, working memory is an area of neurocognitive functioning consistently reported by parents to be a concern in children with sleep problems (Biggs et al., 2011) and there is mounting evidence to indicate that persistent sleep problems in children may have a negative impact on their working memory (for a review see Astill, Van der Heijden, Van IJzendoorn, & Van Someren, 2012). However, the extent to which sleep problems impact on working memory performance in children still remains unclear. This study extends the literature by examining, in depth, the relationship between sleep and
working memory in children, and the specific mechanisms that may underlie any association found.

Sleep problems found in children are most commonly divided into dysomnias and parasomnias (American Psychiatric Association [DSM-IV-TR], 2000). Dysomnias are disorders of initiating or maintaining sleep, which result in impairments in the duration, quality, or timing of sleep (DSM-IV-TR, 2000). Within the dysomnias, sleep breathing disorders (e.g., obstructive sleep apnoea syndrome) account for the majority of clinical referrals for sleep difficulties in children (Moore, Allison, & Rosen, 2006). Other common dysomnias include restless leg syndrome, narcolepsy, insomnia, and periodic limb movement disorder (Moore et al., 2006). Parasomnias are disorders characterised by undesirable physiological, cognitive, or behavioural disruptions that occur predominantly during the sleep-wake cycle (DSM-IV-TR, 2000). The most common parasomnias in children include sleepwalking disorder, night terror disorder, nightmare disorder, enuresis (bedwetting), somniloquy (sleep talking), and sleep bruxism (teeth grinding) (Laberge, Tremblay, Vitaro, & Montplaisir, 2000).

Sleep problems have been associated with decreased performance for a number of children’s cognitive functions including short-term memory, attention, processing speed, and inhibition (Beebe, Wells, Jeffries, Chini, Kalra, & Amin, 2004; Calhoun et al., 2012; Moore et al, 2006; Saunamaki & Jehkonen, 2007; Vriend, Davidson, Corkum, Rusak, Chambers, & McLaughlin, 2013). Mechanisms by which sleep problems contribute to cognitive deficits in children, however, remain open to conjecture. There are two, key, theoretical viewpoints that form the basis of many of the mechanistic models (Alhola & Polo-Kantola, 2007). The first of these suggests that the excessive daytime sleepiness associated with sleep problems in children impairs attention and arousal resulting in decreased cognitive performance (Alhola & Polo-Kantola, 2007). Attention and arousal are thought to be reduced through lapses, slowed responses, and
wake-state instability (Dorrian, Rogers, & Dinges, 2005). Critics of this view, however, argue that the effects of simple daytime sleepiness are often rapidly reversible through interventions such as caffeine and naps, which is incongruent with some of the more persistent cognitive deficits seen in children with obstructive sleep apnoea syndrome (Beebe & Gozal, 2002). The second theoretical viewpoint suggests the effects of poor sleep (e.g., hypoxia due to extreme snoring, sleep disruption) lead to alterations in normal synaptic functioning resulting in neuronal injury within several brain regions (Alhola & Palo-Kantola, 2007; Biggs, Nixon, & Horne, 2014; Kheirandish & Gozal, 2006). Beebe and Gozal (2002) proposed an influential model based on this viewpoint, which suggests the prefrontal cortex is particularly vulnerable to neuronal injury from poor sleep, which is manifest in both adults and children as executive dysfunction (Biggs et al., 2014).

While there are several other competing mechanistic models, a common theme occurring across many is that the functioning of the prefrontal cortex may be particularly sensitive to impaired sleep (e.g., Horne, 1993; Dahl, 1996; Muzur, Pace-Schott, & Hobson, 2002). If this is the case, then one would expect neurocognitive functions that rely heavily upon this region of the brain likewise to be particularly sensitive to impaired sleep. Working memory is one such function where performance has been linked predominantly to heightened neural activity in the prefrontal and parietal regions, based on lesion and brain imaging studies (Funahashi & Kubota, 1994; Smith, Jonides, & Koepppe, 1996). However, to date, the literature on the relationship between sleep and working memory in children remains inconclusive, with some studies finding significant deficits in performance on both subjective and objective measures of sleep and working memory (e.g., Bourke et al., 2011; Halbower et al., 2006; Steenari, Vuontela, Paavonen, Carlson, Fjallberg, & Aronen, 2003) and others not (e.g.,
Support for a causal role of sleep in children’s working memory performance comes from Giordani and colleagues (2012), who performed a follow-up study on a group of 5 to 12 year-old children 1 year post adenotonsillectomy. The researchers initially provided baseline neuropsychological assessments for children with mild to moderate sleep disordered breathing (SDB) awaiting surgery, and compared their performance to a healthy control group (Giordani et al., 2008). The mild SDB group performed less well on a number of tasks including a working memory task, when compared to the control group. No group differences were found between the moderate SDB group and the control or mild SDB group. Follow-up assessment (2012) revealed (regardless of SDB severity and taking into consideration practice effects and normal development) that performance on the working memory tasks had significantly improved. Conversely, Kohler and colleagues (2009) found no significant differences in working memory performance in their sample of children with SDB aged 3 to 12 years, from baseline to follow-up assessment at six months post adenotonsillectomy. The results from the study’s baseline assessments did, however, provide support for an association between sleep and working memory performance, in that children with SDB performed less well on measures of working memory when compared to the control group. While no evidence of a causal relationship was found, the investigators noted that the six month time period between surgery and follow-up assessment may not have been sufficient to observe any positive changes in cognitive outcomes.

Further support comes from studies investigating typically developing children with and without sleep disorders (e.g., Bourke et al., 2011; Buckhalt, El-sheik, & Keller, 2007; Halbower et al., 2006; Steenari et al, 2003; Vriend et al., 2013). A meta-analysis in 2012 (Astill et al.) examined the associations between sleep and cognitive
performance in typically developing, school-aged children. The investigators found shorter sleep duration was associated with deficits in executive function as measured by inhibitory control, cognitive flexibility, and working memory tasks. More recently, Vriend and colleagues (2013) investigated moderate changes in sleep duration in a group of school-aged children, and measured aspects of their behavioural and cognitive functioning including working memory. Children were assigned to one of two groups in which sleep duration was increased or decreased by one hour for four consecutive days. Conditions were then reversed for each child. Results indicated that working memory performance was impaired in the shorter sleep condition, relative to the longer sleep condition, suggesting that even short-term changes to sleep duration can impact upon a child’s working memory. A number of studies have also found associations in typically developing school-aged children between working memory deficits and reduced sleep efficiency, obstructive sleep apnoea, and primary snoring (e.g., Bourke et al., 2011; Buckhalt et al., 2007; Halbower et al., 2006; Steenari et al., 2003).

Critically, however, a similar number of studies have failed to find an association between sleep and working memory performance in typically developing school-aged children (e.g., Archbold et al., 2004; Beebe et al, 2004; Biggs et al., 2011; Calhoun et al., 2009; Sadeh, Gruber, & Raviv, 2003; Vriend, Davidson, Corkum, Rusak, McLaughlin, &Chambers, 2012). For example, similar to Vriend et al. (2013), Sadeh and colleagues manipulated sleep duration; however, children were only assigned to either a one-hour sleep extension or one-hour sleep restriction condition with no reversal of conditions. The researchers failed to find a significant difference in working memory performance between the two groups following the manipulation. Interestingly, Vriend and colleagues (2012) failed to find an association between poor sleep and working memory performance when simply measuring children’s sleep via actigraphy, with no experimental manipulation. The researchers did note, however, that their small
sample size and lack of variability in sleep parameters were distinct limitations to their study.

What is clear after reviewing the literature is that there are a number of methodological problems and inconsistencies across studies, which make it difficult to interpret the relationship between sleep and working memory in children. Problems that are evident across studies include small sample sizes, participants who were not randomly selected from the population (or who were only taken from one specific clinical setting e.g., awaiting adenotonsillectomy), and lack of control groups. Further, a number of the above studies failed to control for confounding variables such as SES and race (e.g., Vriend et al., 2012; Sadeh et al., 2003), both of which have been found to be associated with increased sleep problems (Buckhalt, et al., 2007; Lumeng, Somashekar, Appugliese, Kaciroti, Corwyn, & Bradley, 2007). The age range of participants was also highly variable across studies, which can potentially skew results, particularly when examining working memory performance in children. Past research has demonstrated that distinct processes involved in working memory emerge at different stages of development (e.g., spontaneous rehearsal), with functioning thought to be relatively intact in school-aged children and to reach adult levels by early adolescence (Gathercole, 1998; Gathercole, Pickering, Ambridge, & Wearing, 2004; Luciana & Nelson, 1998). It is possible that when including an age range spanning across early childhood through to adolescence in the one sample (as in Halbower et al., 2006), the processes being activated and measured will not be the same across the different ages.

A further key inconsistency was the definition and operationalisation of working memory, which could be a possible reason for the heterogeneity of results across studies. A number of different tasks have been used to measure the same construct, each differing in their complexity and the cognitive operations required for successful completion. For example, studies have used different complex span tasks (e.g.,
Halbower et al., 2006), n-back memory tasks (e.g., Biggs et al., 2011; Steenari et al., 2003), sequencing and digit span tasks (e.g., Giordani et al., 2008; Kohler et al., 2009) and parent-rated questionnaires such as the Behaviour Rating Inventory of Executive Function (BRIEF) questionnaire (e.g., Bourke et al., 2011, Biggs et al., 2011). It is difficult to generalise results across studies, when different tasks are placing different demands on participants’ working memory and, in turn, activating different processes. For example, a 1-back task requires only simple storage of task relevant information, whereas a complex span task requires both storage and mental manipulation of stimuli, and therefore, is likely to place a greater demand on working memory when compared to the 1-back task.

Furthermore, it is difficult to generalise results across studies using tasks tapping different content domains (verbal and nonverbal) of working memory. The verbal and nonverbal components of working memory are thought to be two related, but separable, systems (Baddeley & Hitch, 1974) and, indeed, several studies (Alloway, et al., 2006; Jarvis & Gathercole, 2003) have found distinguishable differences between verbal and nonverbal working memory systems in both adults and children. For this reason, comparing results across studies that have used tasks that require the use of different modalities may be problematic. Good practise would be to include both, as working memory is a complex cognitive construct with multiple components.

Indeed, research by Bayliss et al. (2003) suggests that a number of separable, basic abilities independently contribute to working memory. To measure working memory performance, Bayliss and colleagues (2003) designed four, complex-span tasks by crossing two types of processing (verbal, visuospatial) with two types of storage (verbal, visuospatial). Independent measures of processing efficiency and storage capacity were also administered to examine the extent to which each contributed to performance on the complex span tasks. Individual differences in both processing speed
and storage capacity accounted for unique variance in working memory performance. Furthermore, the authors found that the residual variance in working memory performance, that remained once variance associated with individual differences in processing speed and storage capacity was removed, was related to higher-order cognition (e.g., reasoning skills). These results are in line with other studies that have found that working memory performance in children is constrained by individual differences from multiple, independent sources including processing speed and storage capacity (e.g., Alloway et al, 2006; Bayliss, Jarrold, Baddeley, & Gunn, 2005). These results suggest that, when assessing individual differences in children’s working memory performance, the unique variance that these cognitive factors contribute should be accounted for by including independent measures of processing efficiency and storage capacity. This, then, should provide a clearer picture of the extent to which sleep impacts on working memory performance, above the impact of sleep on processing speed or storage capacity.

As such, the primary purpose of the present study was to extend the literature in a novel manner, by investigating the contributions of storage capacity and processing speed to any association found between working memory and sleep. The study aimed to overcome the limitations of previous studies and strengthen the construct measurement of working memory by using complex verbal and nonverbal working memory tasks, in addition to independent measures of processing speed and storage capacity. Further, the study also included measures of a wide range of common sleep problems in children in order to obtain a clearer understanding of the specific sleep problems associated with working memory performance in typically developing, school-aged children.

A secondary purpose of the study was better to understand the mechanisms underlying the impact of sleep on working memory, by using a measure of children’s daytime sleepiness as a covariate. Clearly, sleep disruption is likely to result in daytime
sleepiness, which in turn is likely to contribute to cognitive dysfunction. By controlling for simple sleepiness, the study aimed to discern whether the impact of poor sleep on working memory was due to decreased arousal and attention manifested as daytime sleepiness, or might be explained by neuronal injury.

Based on a review of the literature, it was expected that greater sleep problems in school-aged children would be associated with poorer working memory performance, and that this association would remain after controlling for the variance contributed by processing speed and storage capacity. Further, given the noted incongruence between persistent cognitive deficits in children with obstructive sleep apnoea and the rapidly reversible effects of daytime sleepiness (Beebe & Gozal, 2002), it was expected that following the removal of the unique variance contributed by daytime sleepiness, sleep problems would remain predictive of working memory deficits. Finally, based on the findings of a number of studies (e.g., Bayliss, et al., 2003; Alloway et al., 2006), both processing speed and storage capacity were expected to each account for unique variance in children’s working memory performance.

Method

Participants

One hundred children, aged 7 to 11 years ($M = 8.72, SD \pm 1.40$), who took part in the University of Western Australia’s Project K.I.D.S. (Kid’s Intellectual Development Study) during July 2011 through to July 2012, were approached to participate in the study. The project recruits children from approximately 42 schools located in and around the Perth metropolitan area. Selected schools are sent information packages that include consent forms, and these are distributed to parents of children who fit the Project K.I.D.S. criteria. Eligibility for participation in the project involves the child meeting the age criterion for that specific year; having no serious neurological disabilities, no major visual or auditory problems; and being able independently to
complete tasks. Additional criteria were that the child was taking no stimulant medication. Children between 7 and 11 year were selected as intact working memory function has been documented in children as young as six (Gathercole & Pickering, 2000; Gathercole, et al., 2004; Towse, Hitch, & Hutton, 1998), and is thought to begin reaching adult capacity during adolescence (Gathercole, 1998; Gathercole, et al., 2004; Luciana & Nelson, 1998). Furthermore, the majority of children are thought to have stopped napping and to have acquired a monophasic sleep pattern by the ages of 4 to 5 years, which does not change again until the onset of adolescence (Oksar & LeBourgios, 2006).

Of the 100 children approached, 78 (32 girls - 41%) were recruited based upon the study’s inclusion criteria and the return of sleep questionnaires. Demographic information and history of any significant medical conditions was provided by parents, and is displayed in Table 1.

Mothers of participants were asked to provide the highest level of educational qualification achieved and, from this information, maternal level of education was collected as a measure of SES. Maternal education was chosen, as it is a commonly used proxy for SES and has been found to be correlated with a number of sleep problems in children (see e.g., Buckhalt et al., 2007). Educational level was not available for 14 (18.2%) of the mothers. The SES index was classified into five categories: completed lower high school, completed upper high school, completed a college or trade certificate/diploma, completed an undergraduate university degree, and completed a postgraduate university degree. As can be seen from Table 1, the majority of children came from homes where the mother had completed an undergraduate university degree.

Participants were reported to have no broken facial bones, dyslexia, intellectual disability, or mental health disorders. One child had a diagnosis of attention deficit
hyperactivity disorder, and was excluded from the study as it was not clear if the child was being treated with psychostimulant medication, which has been found to affect sleep in some children (Owens, 2009). A small percentage of children were described by parents as currently having learning difficulties. These learning difficulties included one child were described as slow to read, a second described as having a comprehension/delay processing/short-term recall problem, and a third having a central auditory/processing disorder. It was decided not to exclude these children in order to gain a true reflection of the general population. Furthermore, the results of the analyses did not vary significantly when the children were excluded. Likewise, children with asthma and a history of tonsillitis were also included. Finally, no child was reported to regularly consume more than the recommended 100 milligrams of caffeine per day (Seifert, Schaechter, Hershorin & Lipshultz, 2011).

Table 1

<table>
<thead>
<tr>
<th>Category</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Education</td>
<td></td>
</tr>
<tr>
<td>Completed up to year 10 of High School</td>
<td>4 (6%)</td>
</tr>
<tr>
<td>Completed High School</td>
<td>7 (11%)</td>
</tr>
<tr>
<td>College or Trade Certificate/Diploma</td>
<td>10 (16%)</td>
</tr>
<tr>
<td>Undergraduate University Degree</td>
<td>30 (47%)</td>
</tr>
<tr>
<td>Postgraduate University Degree</td>
<td>13 (20%)</td>
</tr>
</tbody>
</table>

**Tasks and Procedures**

Each child was tested over two consecutive days. Testing was embedded within a fun, activity-day format.
Working memory measures

The Letter Number Sequencing subtest (LNS) from the Wechsler Intelligence Scale for Children – 4th Edition (Wechsler, et. al., 2004; WISC-IV) was used to measure verbal working memory. The task requires the participant to store a sequence of 2 to 9 numbers and letters temporarily (e.g., 1, B, 3, G, 7), and then to reorganise the information, speaking aloud the numbers first in ascending order, followed by the letters in alphabetical order (e.g., 1, 3, 7, B, G). The sum of the number of correctly produced sequences was taken as the test score. The LNS is a widely accepted measure of working memory (Economou, 2009; Shelton, Elliott, Hill, Calamia, & Gouvier, 2009) and is considered a gold standard measure of working memory in children (Tulsky, Carlozzi, Chevalier, Espy, Beaumont, & Mungas, 2013). LNS is theorised to draw upon the central executive and the phonological loop due to the necessity of simultaneous storage and manipulation in order to successfully complete the task.

To measure spatial working memory, a computer-based, visual search task was used. Each trial began with 16 boxes (3.2cm by 3.2cm) on the computer screen, filled with 15 distractor stimuli (a red creature with a centered eye or a blue creature with its eye on the right) and the target stimulus (a red creature with its eye on the right). Participants were given 3.5 seconds to search for and click on the target stimulus. Following a response or the lapse of the time limit, the distractor stimuli disappeared from the screen leaving the target stimuli in place for a further 4.5 seconds to allow for the participant to have the opportunity to encode its location on the screen. After a series of search trials, a visual mask was displayed for 1 second, and then participants were required to recall the locations of the target stimuli, in serial order. Participants were provided with three practice trials, four lead-up trials to help the participant reach their working memory capacity before the experimental trials, and 12 experimental trials. The number of target stimuli in each trial increased and decreased adaptively by one
depending on the accuracy of recall on the previous trial. A working memory score was calculated as the average number of target stimuli presented across the experimental trials minus 0.5.

**Storage capacity measures**

The Digit Span Forwards subtest from the WISC-IV was used to measure verbal, short-term storage capacity. The task requires the participant to store a string of 2 to 9 numbers temporarily, and repeat each string back, aloud in serial order. The sum of the correct number of strings was taken as the test score.

To measure spatial storage capacity, a computer-based short-term memory task was used, similar to the spatial working memory task previously mentioned. In the task, 16 squares (3.2cm by 3.2cm) were located in random positions on the computer screen. On each trial, stimuli were presented sequentially in one of the 16 squares for 1 second. At the end of each trial, a visual was displayed for 1 second, and then participants were required to recall the locations of the stimuli in serial order by clicking on the appropriate boxes. The stimuli and the scoring procedures were the same as for the spatial working memory task.

**Processing speed**

The Coding and Symbol Search subscales from the WISC-IV were used as measures of processing speed. The Coding subtest requires children to match symbols with digits contained in a key. The Symbol Search subtest requires the participant to decide whether target symbols match the symbols provided. Both tasks are timed, and correctly matched items were summed and taken as the test scores respectively for each subtest. A combined score of the two subscales was used as a processing speed measure.

**Sleep measure**

The Sleep Disturbance Scale for Children (Bruni et al., 1996; SDSC) was completed by parents and used to measure children’s sleep patterns. The SDSC is a 26-
item questionnaire which produces a total sleep score (TSS) and six subscales: difficulty in initiating and maintaining sleep (DIMS), sleep breathing disorders (SBD), disorders of arousal (DA), sleep–wake transition disorders (SWTD), sleep hyperhydrosis (night sweats; SHY) and disorders of excessive somnolence (DOES). Parents respond on a Likert scale ranging from 1 through to 5, with higher scores on the total sleep score and the six sleep subscales indicating poorer sleep. The DOES subscale, which measures excessive morning and daytime sleepiness, was used to control for everyday sleepiness. Consequently, the TSS was calculated minus the DOES subscale. The SDSC has standardised norms, and displays adequate diagnostic accuracy (Bruni et al., 1996). Bruni and colleagues (1996) reported Cronbach’s alpha of .79 for the control group and .71 for the sleep disordered children’s group, indicating a strong level of internal consistency among the 26 items. However, several of the subscales did not meet the present study’s Cronbach’s alpha criterion (α ≥ .60) which can be seen in Table 2 and, as such, were excluded from the analyses. The TSS, DA, and DOES were included in the statistical analyses. A few data points were missing from seven participants. Little’s MCAR test indicated the values were missing completely at random, $\chi^2 (98) = 104, p > .05$, and Estimation Maximisation was used to replace the values.
Table 2

*Cronbach’s Alpha Coefficients*

<table>
<thead>
<tr>
<th>Sleep Variable</th>
<th>α</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty in Initiating and Maintaining Sleep (DIMS)</td>
<td>.50*</td>
</tr>
<tr>
<td>Sleep Breathing Disorders (SBD)</td>
<td>.28*</td>
</tr>
<tr>
<td>Disorders of Arousal (DA)</td>
<td>.77</td>
</tr>
<tr>
<td>Sleep–Wake Transition Disorders (SWTD)</td>
<td>.39*</td>
</tr>
<tr>
<td>Sleep Hyperhydrosis (SH)</td>
<td>.53*</td>
</tr>
<tr>
<td>Disorders of Excessive Somnolence (DOES)</td>
<td>.67</td>
</tr>
<tr>
<td>Total Sleep Score minus DOES subscale</td>
<td>.61</td>
</tr>
</tbody>
</table>

*Note.* *α* = excluded from analysis as Cronbach’s alpha < .60

**Results**

Prior to analyses, all variables were examined for outliers and deviations of normality. Based on cut-off criteria recommended by Curran, West, and Finch (1996) suggesting a maximum skew of 2 and a maximum kurtosis of 7, analysis revealed the DA variable was not normally distributed. Consequently, a log transformation was used to establish a normal distribution for the variable. An alpha cut-off level of .05 was used in all inferential statistics, and one-tailed *p* values were used for correlational analyses.

In order to gauge the level of sleep problems found within the sample, participants’ scores on the DA and DOES subscales (there were no norms for the Total Sleep Score minus DOES subscale) were converted to T scores (*M* = 50, *SD* = 10) based on the standardised normative values (for ages 6.5 – 15.3 years) provided by Bruni et al (1996). Clinical levels of sleep problems were then determined based on criteria used by Blunden and colleagues (2005) when administering the same sleep scale, (T-score ≥ 67). Only a small percentage of participants met criteria for clinical significant sleep problems. 11 children (14.10%) met criteria for clinical levels of disorders of arousal,
and 3 children (3.8%) met criteria for clinical levels of daytime sleepiness. Of note, no norms were available for our total sleep score measure due to the removal of the DOES items; however, when calculated with the DOES items, there were no participants who had clinically elevated levels of sleep problems.

Table 3 displays the descriptive statistics of the sleep and cognitive variables.

### Table 3

**Descriptive Statistics for Sleep and Cognitive Variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digit Span Forward</td>
<td>77</td>
<td>8.06</td>
<td>1.95</td>
</tr>
<tr>
<td>Digit Span Backward</td>
<td>78</td>
<td>6.63</td>
<td>1.78</td>
</tr>
<tr>
<td>Letter Number Sequencing</td>
<td>77</td>
<td>16.17</td>
<td>3.80</td>
</tr>
<tr>
<td>Processing Speed</td>
<td>77</td>
<td>10.74</td>
<td>3.20</td>
</tr>
<tr>
<td>Spatial Short-Term Memory</td>
<td>75</td>
<td>3.60</td>
<td>0.93</td>
</tr>
<tr>
<td>Spatial Working Memory</td>
<td>76</td>
<td>2.75</td>
<td>1.14</td>
</tr>
<tr>
<td>Disorders of Arousal</td>
<td>78</td>
<td>3.56</td>
<td>1.17</td>
</tr>
<tr>
<td>Disorders of Excessive Somnolence</td>
<td>78</td>
<td>6.82</td>
<td>2.26</td>
</tr>
<tr>
<td>Total Sleep Score minus DOES</td>
<td>78</td>
<td>29.54</td>
<td>4.97</td>
</tr>
</tbody>
</table>

*Note. DOES = Disorders of Excessive Somnolence **Higher scores indicate poorer sleep. For ease of interpretation, values are displayed for the DA before it was transformed. ¹ = data were unavailable for 1 participants; ² = data were unavailable for 3 participants. ³ = data were unavailable for 2 participants.*

A series of one-way ANOVAs examining SES, and a series of independent t-tests with gender as the factor, revealed no significant effects of SES or gender on the cognitive or sleep measures. Consequently, it was not necessary to control for these variables. Table 4 displays the correlations between the age, sleep, and cognitive variables. One-tailed Pearson bivariate correlations revealed that increasing age was significantly correlated with better digit span forward, digit span backward, letter-number sequencing, spatial working memory, and spatial short-term memory. This was expected, as these variables contained data that were not scaled to age.
A one tailed partial bivariate correlation (controlling for age and DOES) was then performed in order to investigate the relationship between the sleep and cognitive variables. The results are shown in Table 5. As expected, all of the cognitive variables were positively associated with each other; however, there were no significant associations between any of the cognitive and sleep variables.
Table 4

Correlations between Age, Sleep Variables, and Cognitive Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age</th>
<th>DSF</th>
<th>DSB</th>
<th>LNS</th>
<th>PS</th>
<th>SSTM</th>
<th>SWM</th>
<th>LogDA</th>
<th>DOES</th>
<th>TSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSF</td>
<td>.35*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSB</td>
<td>.42**</td>
<td>.50**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LNS</td>
<td>.41**</td>
<td>.38**</td>
<td>.33**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS</td>
<td>-.10</td>
<td>.23*</td>
<td>.20*</td>
<td>.42**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSTM</td>
<td>.61**</td>
<td>.55**</td>
<td>.52**</td>
<td>.58**</td>
<td>.23*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SWM</td>
<td>.54**</td>
<td>.40**</td>
<td>.40**</td>
<td>.56**</td>
<td>.32*</td>
<td>.65**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LogDA</td>
<td>.14</td>
<td>.09</td>
<td>.07</td>
<td>.02</td>
<td>.08</td>
<td>-.01</td>
<td>.10</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOES</td>
<td>.09</td>
<td>.05</td>
<td>.21</td>
<td>-.06</td>
<td>-.05</td>
<td>.04</td>
<td>-.01</td>
<td>.12</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>TSS</td>
<td>.08</td>
<td>-.06</td>
<td>.09</td>
<td>-.10</td>
<td>-.05</td>
<td>-.04</td>
<td>.01</td>
<td>.50**</td>
<td>.38**</td>
<td>1</td>
</tr>
</tbody>
</table>

Note. DSF: digit span forward, DSB: digit span backward; LNS: letter number sequencing, PS: processing speed, SSTM: spatial short-term memory, SWM: spatial working memory, LogDA: arousal disorders, TSS: total sleep score. *p < .05, **p < .001, one-tailed
Table 5

*Partial Bivariate Correlations (controlling for Age, and sleepiness: DOES) between Sleep Variables and Cognitive Variables*

<table>
<thead>
<tr>
<th>Variable</th>
<th>DSF</th>
<th>DSB</th>
<th>LNS</th>
<th>PS</th>
<th>SSTM</th>
<th>SWM</th>
<th>LogDA</th>
<th>TSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSF</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSB</td>
<td>.42**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LNS</td>
<td>.29*</td>
<td>.22*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS</td>
<td>.28*</td>
<td>.28*</td>
<td>.51**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSTM</td>
<td>.46**</td>
<td>.38**</td>
<td>.43**</td>
<td>.37*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SWM</td>
<td>.27*</td>
<td>.25*</td>
<td>.42**</td>
<td>.44**</td>
<td>.49**</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LogDA</td>
<td>-.15</td>
<td>&lt;-.01</td>
<td>-.07</td>
<td>.10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSS</td>
<td>-.10</td>
<td>-.01</td>
<td>-.11</td>
<td>-.03</td>
<td>-.11</td>
<td>-.36</td>
<td>.49**</td>
<td>1</td>
</tr>
</tbody>
</table>

*Note. DSF: digit span forward, DBS: digit span backward; LNS: letter number sequencing, PS: processing speed, SSTM: spatial short-term memory, SWM: spatial working memory, LogDA: arousal disorders, TSS: total sleep score. * p < .05, ** p < .001, one tailed*
Discussion

We aimed to provide a comprehensive investigation of the relationship between sleep and working memory performance in a sample of typically developing, school-aged children, by including multiple measures of both working memory and sleep problems. It was expected that sleep problems would predict deficits in working memory performance, and that this relationship would remain following the removal of unique variance contributed by processing speed, storage capacity, and daytime sleepiness. The results from our study did not support this. No association was found between sleep and working memory performance in our sample.

These results are consistent with Sadeh et al. (2002) and Vriend et al. (2012) who both looked at a similar, healthy, school-aged population, and also failed to find a relationship between sleep and working memory. However, while it may be that sleep problems are not associated with working memory performance in typically developing children and that the study’s results are correct; there are a couple of limitations that may have affected the results. First, as can be seen from Table 3, there was very little variability in participants’ scores within the sleep parameters. Only a small number of participants scored at clinically significant levels of sleep problems, while the majority scored consistently within the mild range. This is consistent with Vriend et al. (2012) who also noted a limitation to their study was the lack of variability in their sleep and cognitive parameters.

This lack of variability may have been due to parents underreporting their children’s sleep problems. Parents can often ignore the presence of sleep problems, or are unaware that particular sleep habits such as snoring can indicate potential sleep disorders (Huang, Chen, Li, Wu, Chao, & Guilleminault, 2004). The sample was selected from a fun, holiday program rather than a clinical setting, so parents had no
specific reason to monitor or be overtly aware of their children’s sleep habits leading up to the study. The inclusion of objective sleep measures such as actigraphy and polysomnography may have been able to circumvent this difficulty. Objective sleep measures such as actigraphy or polysomnography are able to provide a more accurate, standardised rating of sleep problems, unlike questionnaires which can be impacted by individual differences in item interpretation and judgement of severity. Further, a number of studies that have found associations between sleep and children’s working memory performance have done so using specific sleep parameters as measured by actigraphy (e.g., Buckhalt et al., 2007; Steenari et al., 2003; Vriend et al., 2013). It may be the indices measured by actigraphy such as sleep duration and sleep efficiency (total time in bed minus total sleep time) are more sensitive measures than those contained within the sleep questionnaire used in the current study. Future studies may want to include both objective and subjective measures of sleep to obtain a more accurate picture of children’s sleep patterns.

Another possible reason for the lack of variability in sleep scores may have been due to the high level of SES within the sample. As is evident from Table 1, almost 70% of participants’ SES scores were in the upper echelons of the SES scale. As mentioned previously, lower SES has been associated with increased sleep problems (Lumeng, et al., 2007) and, as such, the study’s sample was less likely to have impaired sleep. Furthermore, SES has been found to act as a moderator between sleep problems and neurocognitive deficits (Buckhalt, et al., 2007), suggesting the sample in the present study may have been resilient to the effects of poor sleep on working memory performance. For example, Buckhalt et al (2007) demonstrated that children from higher and lower SES had similar cognitive functioning when sleep quality was ideal. However, when sleep quality was poor in both groups of children, children from higher SES had better performance, indicating that children from lower SES may be more
vulnerable to the effects of poor sleep. Future research involving children from a wider range of levels of SES is needed to confirm whether the failure to find a relationship was due to a disproportionate number of children from high SES families.

One of the strengths of the study was in its use of both verbal and nonverbal working memory, processing speed and storage capacity measures. The inclusion of these measures allowed for a systematic investigation, whereby the underlying relationships of working memory could be pulled apart, and the components held accountable for their contributions of variance to working memory performance. This in turn, would have provided us with a clearer picture of the relationship between sleep and working memory. A further strength of the study was the inclusion of a measure of daytime sleepiness, which would have allowed us to provide commentary on the mechanisms by which sleep impacts upon children’s cognition. An understanding of the causal mechanisms underlying the relationship between sleep and cognition means that research can be theory driven, which will in turn decrease the variability of methodologies used across studies as noted above, and potentially reduce the inconsistency in results. Other strengths of the study were that confounding variables were considered and controlled for, and a wide range of sleep problems were included in the TSS subscale.

In summary, this study found no association between parent-reported sleep problems and working memory performance. Future studies may want to ensure a sample that contains children from a wider range of SES and, when investigating working memory, it is recommended to include separate measures of processing speed and storage capacity to account for their unique variance contributed to children’s working memory performance. The inclusion of both verbal and spatial working memory measures will also ensure an exhaustive analysis of working memory performance. Finally, it is recommended that future studies use both objective and
subjective measures of sleep to ensure the maximum sensitivity of measures to sleep problems.

References


Chapter 5:

Sleep and Working Memory in Children with Neurological Conditions

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Abstract

The objective of this study was to investigate whether sleep problems might account for the increased working memory deficits observed in school-aged children with neurological conditions. We chose to take a novel, transdiagnostic approach to our investigation, and treat sleep as a process that could potentially account for working memory difficulties across a range of neurological conditions. Prevalence estimates of sleep problems were also examined. Archival data of 237 children aged 6 to 11 years was collected from a Western Australian state-wide neuropsychological service between July 26, 2011, and January 14, 2014. Measures of parent-reported sleep quality, snoring, and daytime sleepiness were obtained, in addition to objective measures of verbal and spatial working memory, storage capacity, and processing speed. Results revealed that over one third of participants were reported to have clinically significant levels of sleep problems, and that poor sleep quality was significantly associated with verbal working memory difficulties. This association remained after partialling out the variance contributed to performance by storage capacity and processing speed, suggesting sleep was impacting upon an executive component of working memory. No other significant associations were observed. Results suggest that poor sleep quality is associated with an executive component of verbal (rather than spatial) working memory in children with neurological conditions. This has implications for the biological mechanisms thought to underlie the relationship between sleep and cognition in children. Results also demonstrate the clinical utility in taking a transdiagnostic approach when investigating sleep and cognition in children with neurological conditions.
Children with underlying neurological conditions have an increased risk of sleep problems compared to healthy, typically developing, same-aged peers (Dorris, Scott, Zuberi, Gibson, & Espie, 2008; Kotagal, 2007). Neurological conditions typically seen in children presenting for neuropsychological evaluation include common childhood disabilities such as epilepsy, autism spectrum disorders (ASD), birth complications (e.g., prematurity), cerebral palsy, mild cognitive disorder, attention deficit hyperactivity disorder (ADHD), fetal alcohol spectrum disorders (FASD), and acquired brain injuries. Based on research investigating individual diagnoses such as autism, the prevalence of sleep problems in children with neurological conditions may be as high as 75 to 80% (Jan et al., 2008).

Sleep problems in typically developing children are known to be associated with difficulties in a number of cognitive domains including attention, short-term memory, processing speed, and learning (Astill, Van der Heijden, Van IJzendoorn, & Van Someren, 2012; Buckhalt, El-sheikh, & Keller, 2007; Vriend, Davidson, Corkum, Rusak, Chambers, & McLaughlin, 2013). Many children with neurological conditions are already vulnerable to cognitive deficits and subsequent learning difficulties by virtue of their primary diagnosis (e.g., see Jensen & Ozonoff, 1999) and may, therefore, be less able to compensate for stressors such as sleep problems than their typically developing peers. Understanding the relationship between sleep and cognitive functioning in this population is critical, as interventions to improve sleep may help to prevent further cognitive decline and reduce academic underachievement.

The focus of the present study was the impact of sleep on working memory performance. Working memory is a temporary storage system that enables the manipulation of information necessary for complex cognitive processing (Baddeley, 1992). Intact working memory is considered key to a child’s cognitive development as it may underpin the cognitive skills necessary for academic attainment and has been found
to be more predictive of scholastic achievement than IQ (Alloway & Alloway, 2010; Alloway, Gathercole, Kirkwood & Elliot, 2009). Critically, children with underlying neurological conditions are at increased risk of working memory difficulties. Working memory difficulties have been demonstrated in children with frontal and temporal lobe epilepsy (Longo, Kerr, & Smith, 2013), cerebral palsy (Jenks, de Moor, & van Lieshout, 2009), ASD (Steele, Minshew, Luna, & Sweeney, 2007), prematurity (Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, & Oosterlaan, 2009), mild cognitive impairment (Schuchardt, Gebhardt, & Maehler, 2010), acquired brain injury (Conklin, Salorio, & Slomine, 2008), FASD (Norman et al., 2013), and ADHD (Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005). Given the importance of working memory for learning and education, understanding the impact of sleep on the working memory performance of children with neurological conditions may shed some light on the noted learning difficulties in this population. That is, the learning difficulties experienced by these children may be explained, in part, by the impact of poor sleep on working memory.

The relationship between sleep and working memory performance in school-aged children with neurological conditions has been investigated in only a limited number of studies focusing specifically on ADHD, epilepsy, and autism. Zambrano-Sanchez and colleagues (2013) found that working memory deficits (as measured by the arithmetic, digit span, and letter number sequencing subtests from the Wechsler Intelligence Scale for Children–Fourth Edition; WISC-IV) were associated with inadequate sleep hygiene and obstructive sleep apnoea-hypopnea syndrome in children with ADHD. Sawyer et al. (2009) found that children with ADHD and sleep problems had significantly lower test scores than children with ADHD and no sleep problems on a number of cognitive tasks, including working memory (as measured by a computerised task similar to an n-back task). In contrast, Mayes and Calhoun (2009) failed to find a
relationship between sleep and working memory (as measured by WISC-III or WISC-IV Freedom from Distractibility/Working Memory Index), in 477 children with autism aged 1-15 years. Likewise, Holley et al. (2014) failed to find an association between sleep and a number of cognitive tasks, including a working memory measure (Automated Working Memory Assessment; Alloway, Gathercole, & Pickering, 2007) in children with epilepsy aged 6 to 13 years. Nor was there any association found in the Holley et al. study (2014) between sleep and an aggregate measure of executive functioning and processing speed. Thus, there is some evidence that sleep problems contribute to or exacerbate the cognitive difficulties experienced by children with a limited range of neurological conditions. However, to date, research is less than conclusive.

The present study extends this literature by taking a novel, transdiagnostic approach to the investigation of sleep and working memory performance in children with neurological conditions. This approach treats sleep as a process that could explain the presence of working memory deficits across a range of neurological diagnoses. A common assumption is that sleep problems are secondary and specific to the primary neurological diagnosis. However, pervasive sleep problems in children with neurological conditions are frequently due to commonly shared disease-related factors (e.g., severity and location of brain anomaly, pain), rather than as a result of any specific neurological diagnosis (Jan & Freeman, 2004; Jan et al., 2008). This shared etiology suggests that sleep problems may not differ markedly across diagnoses and, as such, it is appropriate to consider neurological conditions collectively when investigating the relationship between sleep and cognition. Whilst a transdiagnostic approach is novel in the sleep and cognition research field, it has been found to be highly useful in the field of mental health, particularly when designing interventions (Egan, Wade, & Shafran, 2012). Clearly, there will be individual differences in the cognitive deficits associated
specifically with individual diagnoses (e.g., tumours, intellectual disability).

Nonetheless, the present study is based on the premise that problematic sleep may explain a proportion of the working memory difficulties children with neurological conditions can experience. A transdiagnostic approach could, potentially, suggest the implementation of an effective treatment/intervention for sleep problems that in turn, results in cognitive benefits across a wide range of neurological conditions (Harvey, 2008).

The first aim of this study was to investigate the prevalence of sleep problems in children with a range of neurological conditions presenting for neuropsychological assessment. This information will be beneficial for clinical practice in that the documented prevalence rates might alert practitioners to the potential usefulness of screening for sleep problems in every child who presents with cognitive deficits, irrespective of diagnosis. While our central goal was to showcase the utility of treating sleep as a transdiagnostic process, prevalence was also calculated by clinical diagnosis (ICD 10) for information purposes and to enable comparison of estimates with other studies investigating individual groups.

The second aim was to investigate the relationship between sleep and working memory performance transdiagnostically, in children with a range of neurological conditions. Parent-report measures of overall sleep quality and snoring were used to assess sleep problems. We focussed on frequency of snoring, rather than sleep breathing disorders (e.g., obstructive sleep apnoea syndrome), as snoring history has been found to be more strongly associated with cognitive performance than other measures of SDB (including those obtained using polysomnography) (Emancipator et al., 2006). Further, habitual snoring is predictive of poor cognition in the absence of sleep breathing disorders and is more prevalent, with base rates of snoring in children estimated to be around 10% compared to OSA, which is present in 1 to 3% of children (Beebe, 2006;
Blunden & Beebe, 2006; Blunden, Lushington, Lorenzen, Martin, & Kennedy, 2005; Rosen, 2004).

We assessed both verbal and spatial working memory, as well as measures of basic processing speed and storage capacity. The inclusion of storage capacity and processing speed measures is fundamental when assessing working memory, as variation in these two basic cognitive abilities has been shown to contribute to individual differences in working memory (e.g., Alloway, Gathercole, & Pickering, 2006; Bayliss, Jarrold, Gunn, & Baddeley, 2003; Conlin & Gathercole, 2006). For example, Bayliss and colleagues (2003) showed that measures of processing speed and storage capacity each explained unique variance in working memory performance. Furthermore, after removing the variance attributable to processing speed and storage capacity, the remaining variance in working memory was associated with higher-order cognition (e.g., fluid intelligence). This residual variance was interpreted by the researchers to represent an executive component of working memory (see also, Jarrold & Bayliss, 2007; Jarrold, Mackett, & Hall, 2014). As studies have also shown that sleep is associated with deficits in both processing speed and storage capacity (e.g., Buckhalt et al., 2007; Sadeh et al., 2003), the inclusion of these measures allowed for the dissection of working memory to uncover which component of working memory, if any, is adversely affected by sleep.

The final aim was to examine the mechanisms by which sleep impacts on children’s cognition. There are two main theoretical approaches within the sleep literature (Alhola & Polo-Kantola, 2007). The first proposes that the excessive daytime sleepiness associated with sleep disorders negatively impacts on attention via arousal, resulting in impaired cognition (Alhola & Polo-Kantola, 2007; Dorrian, Rogers, & Dinges, 2005). Accordingly, we included a measure of daytime sleepiness to assess whether this may be contributing to any relationship found between sleep problems and
working memory. However, given the effects of daytime sleepiness are often easily reversible by treatments such as caffeine and naps, while some of the cognitive deficits evident in children with sleep breathing disorder are quite pervasive (Beebe & Gozal, 2002), it was expected that daytime sleepiness would not be the sole mechanism by which sleep impacts upon cognition (Beebe & Gozal, 2002).

The second theoretical approach proposes that the specific effects of sleep problems (e.g., hypoxia and sleep disruption) lead to alterations in synaptic functioning and consequent neuronal injury, particularly in the prefrontal cortex, manifest behaviourally as executive dysfunction (Alhola & Palo-Kantola, 2007; Beebe & Gozal, 2002; Horne, 1993). The inclusion of the processing speed and storage capacity measures allowed us to explore the relationship between the executive component of working memory and sleep problems more directly. The rationale was that if sleep problems remain predictive of children’s working memory performance after accounting for the variance associated with daytime sleepiness, storage capacity, and processing speed, this would suggest that disordered sleep is selectively impacting upon an executive component of working memory. Moreover, the inclusion of both verbal and spatial working memory measures allowed us to determine whether the effect of sleep upon working memory is domain general, as would be predicted by mechanistic accounts preposing sleep-related neuronal injury to the prefrontal cortex (e.g., Beebe and Gozal, 2002; Horne, 1993).

Method

Participants

Archival data were obtained from the records of 237 children (82 female; \( M_{\text{age}} = 8.08 \text{ year}, SD = 1.65, \text{ range: 6.0 to 11.11 years} \) who were consecutively assessed at a Western Australian state-wide neuropsychological service between July 26, 2011, and January 14, 2014. The Neurosciences Unit provides clinical services within the
context of a multi-disciplinary team for children aged 5 years and over, who have a known or suspected brain impairment resulting from trauma, disease or genetic conditions. The service collects routine clinical data evaluating presenting difficulties across neurocognitive, behavioural, affective and social domains. Records were accessed only for those children whose parents had signed consent forms for their children’s data to be used in a research setting. Of these, children were included if they had completed both sleep and either of the two working memory measures (e.g., verbal or spatial). The data collected included neuropsychological test scores and questionnaire data. Approval for this study was granted by the North Metropolitan Health Service – Mental Health and University of Western Australia Human Research Ethics Committees.

All children had one or more diagnoses based on the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (World Health Organisation, ICD 10). Participants were grouped into 13 categories based on their primary diagnosis: congenital malformations of the brain; mild cognitive disorders (also known as intellectual disability); birth complications (e.g., being born preterm); epilepsy; acquired brain injury or infection; cerebral palsy, hemiplegia, and other motor disorders; specific developmental disorders; pervasive developmental disorders; foetal alcohol spectrum disorders; attention deficit hyperactivity disorders; chromosomal abnormalities; psychological-related diagnoses (e.g., depressive disorder); cancer; or other medical problems (see Table 6). Socioeconomic status (SES) was included as a potential confounding variable, as lower SES is associated with greater sleep problems in children (see e.g., Buckhalt et al., 2007). Level of maternal education was used as a proxy for SES. Level of education was not available for 44 of the participants’ mothers (18.6%); 57 (24.1%) mothers had completed up to year 10 of high school; 31 (13.1%) high school; 49 (20.7%) a college or trade certificate/diploma; 45 (19.0%) an
undergraduate university degree; and 11 (4.6%) had completed a postgraduate university degree.

**Tasks**

*Working memory measures*

Digit Span Backwards from the Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV) was used to assess verbal working memory. The backward digit span task requires information to be stored and manipulated, placing a demand on working memory and thus making the task more sensitive to working memory deficits. This simultaneous storage and processing is thought to place direct demands on the central executive (Henry, 2012). The total number of correctly produced strings was taken as the test score.

Spatial Span Backwards from the Wechsler Nonverbal Scale of Ability (WNV; Wechsler & Naglieri, 2006) was used as a measure of spatial working memory. Backward spatial span is regarded as a measure of spatial working memory because not only must multiple units of information be stored and recalled, but they must be reverse-ordered (manipulated) in memory before the participant can respond (Luciana, Conklin, Hooper, & Yarger, 2005). This test is designed for children eight years and above, so scores were available for these children only (see Table 2). The subtest has good reliability ($\alpha = .77-.85$) across the age groups in the present study (8 to 11 years). The total number of correctly produced sequences was taken as the test score.

*Storage capacity measures*

Digit Span Forwards from the WISC-IV was used as a measure of verbal, short-term storage capacity. The total number of correctly produced strings was taken as the test score.

Spatial Span Forwards from the WNV was used to measure spatial storage capacity. The total number of correctly produced strings was taken as the test score.
**Processing speed**

The Coding and Symbol Search subscales from the WISC-IV were used as measures of processing speed. A composite index score derived from the summed, age-scaled scores from the two subscales was used as a processing speed measure. Raw scores were not used as Coding and Symbol search scores must be age-scaled before combining them to form the WISC-IV Processing Speed Index.

**Sleep measures**

The Sleep Disturbance Scale for Children (Bruni et al., 1996; SDSC) was used to assess children’s sleep patterns. The SDSC is a 26-item, parent-rated questionnaire which produces a total sleep score and six subscales: difficulty in initiating and maintaining sleep (DIMS), sleep breathing disorders (SBD), disorders of arousal (DA), sleep–wake transition disorders (SWTD), sleep hyperhydrosis (night sweats; SH), and disorders of excessive somnolence (DOES). Parents respond on a Likert scale ranging from 1 ‘Never’ to 5 ‘Always (daily)’, with higher scores indicating poorer sleep. The total sleep score, the DOES subscale, and the snoring item from within the SBD subscale were used in the following analyses. These sleep items were selected to assess sleep quality, daytime sleepiness, and snoring respectively. Raw scores were used for each sleep measure (including snoring). The total sleep score was calculated without the DOES subscale in order to tease apart the effects of sleep quality and daytime sleepiness, but with the DOES subscale in order to obtain scaled scores from the norms provided by Bruni et al. (1996) for calculating prevalence rates. After age-scaling each total sleep score, clinical levels of total sleep problems were then determined based on the criteria used by Blunden et al. (2005) of a t score ≥ 67. We applied the same procedure and clinical cut-off scores to the DOES measure to obtain prevalence rates of excessive daytime sleepiness. Children were also classified as snorers or non-snorers based on Blunden and colleague’s (2005) criteria, whereby children who snored 1-5
times per week were considered snorers, and those who snored occasionally (not at all, \( \leq 1 \) or 2 times per month) were categorised as non-snorers.

The SDSC has standardised norms and strong reliability, with Bruni and colleagues (1996) reporting Cronbach’s alpha of .79 for a control group and .71 for a sleep disordered children’s group. The present study set a minimum Cronbach’s alpha criterion of \( \alpha \geq .60 \) (Nunnally & Bernstein, 1994). Both the total sleep score (\( \alpha = .82 \)) and DOES (\( \alpha = .76 \)) measures met this criterion. 1.7\% (91 values) of the SDSC data were missing. Although the proportion missing transdiagnostically was small, Little’s MCAR Test indicated that the values were not ‘missing completely at random’, \( \chi^2 (737) = 910.24, p < .001 \), which potentially had repercussions for prevalence estimates that were based on smaller sample sizes within ICD 10 groups. Independent \( t \) tests were run transdiagnostically, to investigate whether there were any differences in scores per sleep item (26 sleep items in total) between the children with missing data points and those without. We found 11 significant differences in sleep scores across the two groups out of a total of 26, with the missing data group reporting significantly higher (increased sleep problems) on all 11 differences. As such, five multiple imputation data sets were generated. Prevalence analyses were run on two datasets: 1) the subset of participants with complete data (i.e., those who completed every DOES item, those with snoring scores, or those who completed every item for the total sleep score); and 2) with all participants using pooled, multiple imputation.

Statistical Analysis

All data were analysed using IBM SPSS statistical program version 22.0. All variables were normally distributed, with no outliers detected. To test for covariates and potential confounders, groups were compared using independent \( t \) tests, analyses of variance (ANOVAs), and Pearson’s bivariate correlations. Prevalence estimates were calculated using percentages. Partial correlations and a hierarchical regression analysis
were used to assess the relationship between the sleep measures and each cognitive outcome, adjusting for potential confounders. An alpha level of .05 was used in all inferential statistics and one-tailed analyses were used in the correlation analyses where directional predictions were made.

**Results**

Table 6 presents the percentage of children with clinical levels of snoring, daytime sleepiness, and total sleep problems both transdiagnostically and within each clinical group, for both the complete and the imputed data sets.

**Table 6**

*Descriptive statistics and percentage of clinically elevated sleep problems across and within diagnostic categories (N=236)*

<table>
<thead>
<tr>
<th>ICD 10 Group</th>
<th>Pooled MI N = 236</th>
<th>Complete Data N = 181-232</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%TSS(N)</td>
<td>%Snoring</td>
</tr>
<tr>
<td>Transdiagnostically</td>
<td>37.4(211)</td>
<td>28.2</td>
</tr>
<tr>
<td>Mild Cognitive Disorder</td>
<td>29.2(13)</td>
<td>46.8</td>
</tr>
<tr>
<td>Birth Complications</td>
<td>23.8(16)</td>
<td>42.2</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>46.9(29)</td>
<td>25.9</td>
</tr>
<tr>
<td>Acquired Brain Injury/Infection</td>
<td>35.3(17)</td>
<td>23.4</td>
</tr>
<tr>
<td>CPHM</td>
<td>14.7(34)</td>
<td>28.3</td>
</tr>
<tr>
<td>SDD</td>
<td>51.6(22)</td>
<td>25.4</td>
</tr>
<tr>
<td>Chromosomal Abnormalities</td>
<td>26.1(23)</td>
<td>26.1</td>
</tr>
</tbody>
</table>

*Note.* CPHM: cerebral palsy, hemiplegia, and other motor disorders; SDD: Specific Developmental Disorders; TSS: total sleep score (including DOES); DOES: disorders of excessive somnolence. Only the clinical groups with 10 or more children are reported.

Although there was variation in the prevalence estimates for total sleep problems derived from the complete and pooled multiple imputation datasets, the estimates derived from snoring and DOES were similar across the two datasets with the true
values believed to lie somewhere in between. Importantly, over one third of our sample was reported to have total sleep problem T-scores in the clinical range. Looking across both data sets, there were a number of specific clinical groups which had prevalence estimates greater than those found transdiagnostically. Of note, the epilepsy group recorded very large estimates (greater than transdiagnostic estimates) for two out of the three sleep categories (daytime sleepiness and total sleep problems) suggesting that these children experience a range of sleep problems to a greater degree than the other groups. Meanwhile, both the mild cognitive disorders group and the birth complications groups recorded prevalence estimates greater than the transdiagnostic estimate for elevated levels of snoring, as did the specific developmental disorders group for total sleep problems.

Following a close inspection of the two data sets, it was decided that all remaining analyses (e.g., excluding prevalence estimates), would be run using the case by case data set rather than the pooled multiple imputation data set, since this was the more conservative. Table 7 displays the descriptive statistics for the cognitive and sleep variables for all participants.
Table 7

Descriptive statistics for the cognitive and sleep variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>M (SD)</th>
<th>Min</th>
<th>Max</th>
<th>Skew</th>
<th>Kurtosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal Digit Span Forwards</td>
<td>198</td>
<td>6.36 (2.07)</td>
<td>0</td>
<td>12</td>
<td>0.14</td>
<td>0.36</td>
</tr>
<tr>
<td>Verbal Digit Span Backwards</td>
<td>198</td>
<td>4.35 (2.21)</td>
<td>0</td>
<td>13</td>
<td>-0.28</td>
<td>1.02</td>
</tr>
<tr>
<td>Spatial Digit Span Forwards</td>
<td>112</td>
<td>5.36 (1.76)</td>
<td>1</td>
<td>11</td>
<td>0.11</td>
<td>0.40</td>
</tr>
<tr>
<td>Spatial Digit Span Backwards</td>
<td>112</td>
<td>4.54 (2.12)</td>
<td>0</td>
<td>10</td>
<td>0.08</td>
<td>-0.40</td>
</tr>
<tr>
<td>Processing Speed Index</td>
<td>171</td>
<td>84.64 (16.10)</td>
<td>21</td>
<td>121</td>
<td>-0.23</td>
<td>0.79</td>
</tr>
<tr>
<td>Disorders of Excessive</td>
<td>188</td>
<td>8.27 (3.47)</td>
<td>5</td>
<td>24</td>
<td>1.54</td>
<td>2.70</td>
</tr>
<tr>
<td>TSS minus DOES*</td>
<td>171</td>
<td>35.93 (9.39)</td>
<td>22</td>
<td>62</td>
<td>0.68</td>
<td>-0.13</td>
</tr>
<tr>
<td>Snoring Item*</td>
<td>208</td>
<td>2.06 (1.17)</td>
<td>1</td>
<td>5</td>
<td>1.04</td>
<td>0.26</td>
</tr>
</tbody>
</table>

Note. TSS minus DOES: total sleep score minus disorders of excessive somnolence. *Higher scores indicate poorer sleep. ¹ = data were unavailable for 34 participants; ² = data were unavailable for 120 participants due to age requirements for the task. ³ = data were unavailable for 61 participants. ⁴ = data were unavailable for 2 participants. ⁵ = data were unavailable for 24 participants.

An independent t test revealed no significant differences between males and females on any of the cognitive or sleep measures. Similarly, ANOVA revealed no significant effects of SES on the sleep or cognitive measures. As such, gender and SES were not included as covariates in subsequent analyses. Pearson bivariate correlations showed older children had better verbal storage capacity, \( r(198) = .26, p < .001 \), spatial working memory, \( r(112) = .25, p = .007 \), and verbal working memory, \( r(198) = .47, p < .001 \). Age was not associated with any of the sleep measures. Based on these findings, age was covaried in all analyses.

Partial correlations were used to examine the relationship between the sleep and cognitive measures whilst controlling for age (Table 8). Total sleep score and verbal working memory were significantly related, with poorer sleep quality associated with poorer verbal working memory. As there was no association between sleep and spatial working memory performance, the spatial measures were dropped from further
analyses. Similarly, no association was found between the snoring and working memory measures, thus, snoring was also removed from further analyses.
Table 8

*Partial Bivariate Correlations (controlling for Age) between Sleep Variables and Cognitive Variables*

<table>
<thead>
<tr>
<th>Variable</th>
<th>SSTM</th>
<th>SWM</th>
<th>VSTM</th>
<th>VWM</th>
<th>PS</th>
<th>Snoring</th>
<th>DOES</th>
<th>TSS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=112</td>
<td>n=112</td>
<td>n=198</td>
<td>n=198</td>
<td>n=171</td>
<td>n=208</td>
<td>n=188</td>
<td>n=171</td>
</tr>
<tr>
<td>SSTM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SWM</td>
<td>.44**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VSTM</td>
<td>.26**</td>
<td>.13</td>
<td>1</td>
<td></td>
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<tr>
<td>VWM</td>
<td>.28**</td>
<td>.16</td>
<td>.51**</td>
<td>1</td>
<td></td>
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<tr>
<td>PS</td>
<td>.44**</td>
<td>.39**</td>
<td>.27**</td>
<td>.36**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Snoring</td>
<td>-.06</td>
<td>.04</td>
<td></td>
<td>-.06</td>
<td>.10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOES</td>
<td>.01</td>
<td>-.03</td>
<td>-.04</td>
<td></td>
<td>-.02</td>
<td>.12</td>
<td></td>
<td></td>
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<tr>
<td>TSS</td>
<td>.03</td>
<td>0</td>
<td>-.09</td>
<td>-.26**</td>
<td>.08</td>
<td>.34**</td>
<td>.39**</td>
<td>1</td>
</tr>
</tbody>
</table>
Hierarchical regression analysis was used to investigate whether daytime sleepiness might be contributing to the observed relationship between sleep quality and verbal working memory. Age was entered in Step 1 in the prediction of verbal working memory. Daytime sleepiness was entered in Step 2, followed by the total sleep score at Step 3. The order of entry of the two sleep measures was then reversed to measure the unique and shared variance accounted for by each variable. The model explained 26.7% of the variance in verbal working memory performance. As can be seen from Table 9, total sleep score remained predictive of verbal working memory performance after the influence of daytime sleepiness was accounted for, explaining 4.2% of unique variance. Daytime sleepiness was not a significant predictor, explaining less than 1% of the variance in verbal working memory performance in our sample.
Table 9

Hierarchical Regression Analyses with Children’s Sleep Quality, Daytime Sleepiness, Storage Capacity, and Processing Speed, Predicting Verbal Working Memory Performance

<table>
<thead>
<tr>
<th>Predictors</th>
<th>B (CI)</th>
<th>β</th>
<th>R²</th>
<th>ΔR²</th>
<th>ΔF (df)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Role of Daytime Sleepiness (N=147)</strong></td>
<td></td>
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<tr>
<td><em>Step 1</em></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Age</td>
<td>.67**(.46 to .87)</td>
<td>.47</td>
<td></td>
<td></td>
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<tr>
<td><em>Step 2</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.67**(.47 to .88)</td>
<td>.48</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOES</td>
<td>-.31 (-.13 to .07)</td>
<td>-.05</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><em>Step 3</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.70**(.50 to .90)</td>
<td>.49</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOES</td>
<td>.04 (-.07 to .14)</td>
<td>.05</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>TSS</td>
<td>-.06*(-.10 to -.02)</td>
<td>-.23</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><em>Steps 2 and 3 Reversed</em></td>
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<td></td>
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<tr>
<td><em>Step 2</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.70**(.50 to .90)</td>
<td>.50</td>
<td></td>
<td></td>
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<tr>
<td>TSS</td>
<td>-.05*(-.09 to -.02)</td>
<td>-.21</td>
<td></td>
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<tr>
<td><em>Step 3</em></td>
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</tr>
<tr>
<td>Age</td>
<td>.70**(.50 to .90)</td>
<td>.49</td>
<td></td>
<td></td>
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<tr>
<td>TSS</td>
<td>-.06*(-.10 to -.02)</td>
<td>-.23</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOES</td>
<td>.04 (-.07 to .14)</td>
<td>.05</td>
<td></td>
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<tr>
<td><strong>Role of Processing Speed and Storage Capacity (N=131)</strong></td>
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<tr>
<td><em>Step 2</em></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Age</td>
<td>.50**(.31 to .68)</td>
<td>.38</td>
<td></td>
<td></td>
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<tr>
<td>DSF</td>
<td>.42**(.26 to .58)</td>
<td>.37</td>
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<tr>
<td>PS</td>
<td>.02*(.01 to .04)</td>
<td>.19</td>
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<td></td>
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<tr>
<td><em>Step 3</em></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Age</td>
<td>.51**(.33 to .69)</td>
<td>.39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSF</td>
<td>.43**(.27 to .59)</td>
<td>.38</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS</td>
<td>.03*(.01 to .04)</td>
<td>.20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSS</td>
<td>-.04*(-.07 to -.01)</td>
<td>-.16</td>
<td></td>
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</tbody>
</table>

*Note. DOES: disorders of excessive somnolence; TSS: total sleep score; DSF: digit span forward; PSI: processing speed index. * p < .05; ** p < .01, one-tailed. For the sake of parsimony, only significant covariates were included in analyses. *

A second, hierarchical regression was conducted to investigate whether sleep quality was predictive of verbal working memory performance, above and beyond any
variance shared with processing speed and storage capacity. As above, age was entered in Step 1. Processing speed and verbal storage capacity were entered in Step 2, followed by the total sleep score in Step 3. The model accounted for 42.7% of the variance in verbal working memory performance. The addition of processing speed and storage capacity accounted for 20.1% of unique variance in verbal working memory performance. Crucially, sleep quality remained a significant predictor following the control of processing speed and verbal storage capacity, explaining 2.6% of unique variance.

**Discussion**

This study investigated the relationship between sleep and working memory in children with neurological conditions, and the mechanisms by which sleep may impact on working memory performance. A transdiagnostic approach was taken. A key finding was the high prevalence of clinically significant sleep problems and snoring among the children in our sample. A second key finding was the unexpected nature of the relationship between sleep and working memory performance, in that our results suggest a domain specific (e.g., verbal, but not spatial), rather than a domain general, association. This has implications for understanding of the mechanisms by which sleep impacts children’s cognition.

**Prevalence**

Over one third of the children in this study were currently experiencing sleep problems in the clinical range, as reported by a parent. Nearly 50% of children with epilepsy were reported to have clinically elevated levels of sleep problems, in addition to almost one third reporting excessive daytime sleepiness. Similarly, nearly 50% of parents of children with specific developmental disorders reported clinically elevated levels of sleep problems, while similar percentages reported elevated levels of snoring in children from the birth complications group and children from the mild cognitive...
disorders group. It is possible that parents over-estimated the level of sleep disturbance in our sample, as has been found in previous studies investigating clinical samples (e.g., Holley et al., 2014; Wiggs, Montgomery, & Stores, 2005). However, our prevalence estimates appear to be in line with estimates from previous studies that typically range between 30 to 70% (for a review see Dorris et al., 2008; Richdale, 1999). In general, sleep disturbance (snoring and total sleep problems) appeared elevated across neurological conditions alike, a finding at odds with the assumption that sleep problems are secondary and specific to individual diagnoses. Rather, our estimates establish that clinically elevated sleep disturbance is a common occurrence across a range of children’s neurological conditions and provide support for a transdiagnostic approach to the investigation of sleep and working memory in this population of children.

Sleep and Working Memory

Further support for taking a transdiagnostic approach when investigating sleep and working memory in children with neurological conditions comes from our finding that poor sleep quality was associated with reduced verbal working memory performance in our sample. Our results are consistent to those of Zambrano-Sanchez et al. (2013) and Sawyer et al. (2009), who both found that problematic sleep was associated with working memory difficulties in children with ADHD. However, our results extend their findings by demonstrating that the sleep and working memory relationship spans across many common childhood neurological conditions, rather than occurring in specific, individual diagnoses. We argue that our findings provide evidence of disturbed sleep as a transdiagnostic risk factor that maintains and exacerbates the working memory difficulties found in children with neurological conditions. The clinical utility in taking a transdiagnostic approach is that practitioners would then screen for sleep problems in all children with neurological conditions and interventions could be put in place early. Early intervention for sleep disturbance in these children,
resulting in even a small change in working memory performance, potentially means that one or several abilities crucial for learning and academic success might be improved, and this might mean the difference between a child passing or repeating a grade.

One interesting finding was that results from the current study do not support an association between sleep and spatial working memory performance. It was expected that any impact of sleep on working memory would reflect a domain general, executive problem. Our findings suggest, however, that the impact of poor sleep is domain specific. Some suggestion of a domain specific effect of sleep also comes from Steenari and colleagues (2003), who found audiospatial working memory performance in typically developing children was more greatly affected by poor sleep quality than performance on a visuo-spatial working memory task. Given that performance on verbal and visuo-spatial working memory tasks is known to activate both common and distinct cerebral areas, our findings suggest that sleep may potentially adversely affect those cerebral areas more closely related to verbal rather than spatial working memory. This is discussed in detail below, along with the mechanisms by which sleep difficulties impact upon children’s cognition.

Results from our study also failed to support a relationship between snoring and cognition. While these results contradict those of previous studies that have found snoring is highly predictive of cognitive and academic performance in school-aged children (e.g., Blunden & Beebe, 2006; Bourke et al., 2011; Emancipator et al., 2006), they are in line with the studies of Biggs and colleagues (2011) and Beebe and colleagues (2004). Beebe and colleagues (2004), who also used the digit span backwards task to measure working memory, suggested that either working memory is not as vulnerable to the effects of sleep breathing disorders as previously thought, or the digit span task lacks sensitivity. While either of these suppositions may explain the lack
of association, it is possible that in the current study, it was our sleep measure that lacked the sensitivity to detect an association in our participants due to the nature of the questionnaire. The SDSC requires parent retrospectively rate their child’s sleep behaviours during the previous six months. We could not ask parents, in advance, to monitor their children’s sleep, and it may be that some children were incorrectly rated as snoring (or not snoring) on our sleep measure, which may explain the lack of an association. To address this limitation, future studies using questionnaires are recommended to have parents begin monitoring their children’s sleep well in advance of the study’s onset.

**Mechanisms**

As mentioned above, the unexpected nature of the relationship between sleep and working memory has theoretical implications for the mechanisms by which sleep impacts upon cognition. Firstly, results from our study do not support the viewpoint that the association between sleep and children’s cognition is due to excessive daytime sleepiness impacting upon attention and arousal. Daytime sleepiness was not predictive of working memory performance in our sample.

However, our results do not lend unqualified support to the viewpoint that disturbed sleep causes global neural injury to the prefrontal cortex either. Instead, it seems that this account may not be specific enough in terms of the prefrontal areas affected by poor sleep in children. Sleep quality remained predictive of verbal working memory following the control of processing speed, and storage capacity, indicating an association between sleep quality and the executive component of working memory and, therefore, potentially an association between sleep and the prefrontal cortex. However, we did not find an association between spatial working memory and sleep, which challenges the supposition that the prefrontal cortex as a whole is impacted by poor sleep.
Taken together, these results suggest that the impact of poor sleep upon the executive component of working memory is specific to the verbal domain, which implies that specific regions of the prefrontal cortex which mediate verbal executive functions (as opposed to spatial) are adversely affected by sleep, rather than the prefrontal cortex in general. This is plausible when one considers that ‘executive function” is an umbrella term encompassing a range of different higher-order cognitive functions, and that the prefrontal cortex is a large, heterogeneous neurological region that has extensive connections with other cortical and subcortical regions (Arsten, 2009; Elliot, 2003). Different regions of the prefrontal cortex have different connections throughout the brain, and verbal and spatial working memory tasks are known to activate different areas (Smith, Jones, & Koepppe, 1996). It may be that sleep impacts on a specific region of the prefrontal cortex that is connected primarily to a cortical or subcortical region necessary for verbal executive functions only. For example, while performance in both domains is known to activate the prefrontal cortex and parietal lobes, spatial working memory tasks are associated with right hemisphere activation and verbal working memory tasks with left (Smith et al., 1996). Further, regional brain activation studies investigating cognitive functioning in adults have shown that certain areas of the brain have decreased activation following sleep deprivation (Durmer & Dinges, 2005). One of these areas is the left temporal lobe, which is usually highly active during verbal working memory tasks only (Drummond, Gillian, & Brown, 2001; Drummond, Brown, Gillian, Stricker, Wong, & Buxton, 2000; Durmer & Dinges, 2005). It may be that sleep-related alterations that occur in the prefrontal cortex are to regions associated with verbal working memory only. However, neuroimaging studies investigating the effects of poor sleep are relatively rare in children and results from adult studies cannot be readily extrapolated to children due to age dependent changes in circadian rhythms and working memory performance (Beebe, 2011; Gathercole,
Pickering, Ambridge, & Wearing, 2004). The inclusion of neuroimaging in future studies is needed to investigate the cerebral regions associated with sleep problems and working memory in children.

Of note, our results were not simply due to more children having impaired performance on the verbal working memory task relative to the spatial task. One advantage of our study was that it allowed for a direct comparison between performance on verbal and spatial working memory tasks using the same children. As there was a similar percentage of children with impaired levels of verbal working memory performance as there was spatial, the failure to find an association between spatial working memory and sleep was not simply due to more children being impaired on the verbal task.

In conclusion, the findings from the present study indicate that poor sleep quality is associated with deficits in verbal working memory performance in school-aged children with neurological conditions, and that this association is not simply as a result of the child being sleepy. Our results underscore the clinical and practical utility of taking a transdiagnostic approach when investigating sleep problems in children with neurological conditions. Moreover, our finding of an association between the verbal executive component of working memory and not spatial, fails to fit with current mechanistic approaches that posit sleep impacts upon the prefrontal cortex as a whole. Instead, our results suggest that sleep-related neuronal injury may be to specific regions of the prefrontal cortex only.

References


Chapter 6:

Sleep and Working Memory in Children Born Very Preterm

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2 School of Psychology and Exercise Science, Murdoch University
3 UWA Centre for Neonatal Research & Education
Abstract

In two studies, we investigated the relationship between sleep and working memory performance in children born very preterm (i.e., gestation less than 32 weeks), and the possible mechanisms underlying this relationship. In Study 1, parent-reported measures of snoring, sleep quality, and daytime sleepiness were collected on 89 children born very preterm aged 6-7 years old. Children completed a verbal working memory task, as well as measures of processing speed and verbal storage capacity. Sleep quality was associated with verbal working memory performance, over and above the variance associated with individual differences in processing speed and storage capacity, suggesting that poor sleep may have its impact on the executive component of working memory. Snoring and daytime sleepiness were not associated with working memory performance. Study 2 examined the impact of sleep problems on executive functioning more directly. Parent reported sleep problems were collected on 43 children born very preterm and 48 typically-developing peers (aged 6 to 9 years). Problematic sleep was found to adversely impact executive functioning in the very preterm group, while no effect of sleep was found in the control group. These findings implicate executive dysfunction as a possible mechanism by which sleep adversely impacts upon cognition in children born very preterm, and demonstrate that sleep problems can increase the cognitive vulnerability already experienced by many of these children.
Sleep problems are frequently reported by parents of school-aged children, with approximately 25% of all children experiencing some form of sleep disturbance (Owens, 2007). Common childhood sleep problems include sleep disordered breathing (SDB; e.g., sleep apnoea, snoring, hypoxia), insomnia, restless legs syndrome, excessive daytime sleepiness, sleep walking, and nightmare disorder (Blunden, Lushington, Kennedy, Martin, & Dawson, 2000; Laberge, Tremblay, Vitaro, & Montplaisir, 2000; Moore, Alison, & Rosen, 2006). Sleep problems negatively impact on a number of neurocognitive functions in typically developing children including attention, inhibition, cognitive flexibility, processing speed, short-term memory, and learning (Beebe, Wells, Jeffries, Chini, Kalra, & Amin, 2004; Calhoun et al., 2012; Moore et al., 2006; Saunamaki & Jehkonen, 2007; Vriend, Davidson, Corkum, Rusak, Chambers, & McLaughlin, 2013). Of particular interest to the current study is the impact of sleep problems on children’s working memory, a cognitive system responsible for temporarily storing and processing information necessary for complex cognitive tasks (Baddeley, 1992). Working memory is of interest, as its limited capacity is strongly predictive of a child’s ability to learn and acquire new skills (Alloway & Alloway, 2010; Alloway, Elliot, Gathercole, & Kirkwood, 2009). Given the importance of working memory for children’s learning, investigating the impact of treatable problems such as poor sleep is crucial. One population of children for whom this investigation is most vital, is children born very preterm (prior to 32 weeks), as this population is known to have both increased sleep problems and working memory difficulties (Clark & Woodward, 2010; Perkinson-Gloor et al., 2015). The identification of an association between sleep and working memory in children born very preterm may lead to targeted sleep interventions that result in improvements in academic ability.

Healthy school-aged children born very preterm are at increased risk of sleep problems when compared to children born to term (Perkinson-Gloor et al., 2015). While
it is unclear why there is such an elevated prevalence of sleep disturbance within the very preterm population, it may result from perinatal or developmental problems associated with respiratory control and upper airway development such as infection, hypoxic ischemia (brain injury caused by oxygen deprivation), intraventricular haemorrhage, and periventricular leukomalacia (PVL) (Aylward, 2005; Inder & Volpe, 2000; Rosen et al., 2003; Taylor, Minich, Bangert, Filipek, & Hack, 2004). When compared to their term counterparts, children born very preterm are also at risk of mild cognitive deficits including difficulties with working memory (Aarnoudse-Moens, Smidts, Oosterlaan, Duivenvoorden, & Weisglas-Kuperus, 2009). Indeed, a number of studies have identified both verbal and spatial working memory deficits in school-aged children born prematurely (Aarnoudse-Moens et al., 2009; Clark & Woodward, 2010; Mulder, Pitchford, & Marlow, 2010). For example, in a meta-analysis investigating neurobehavioral outcomes in children born very preterm, working memory performance was significantly poorer in children born very preterm and/or low birth weight compared to controls (Aarnoudse-Moens et al., 2009). Moreover, these deficits persist. In a separate study comparing executive functioning in very preterm and term children aged 4 to 12 years, working memory deficits were evident in children born very preterm, regardless of age (Aarnoudse-Moens et al., 2012). Relative to term children, children born very preterm performed within the normal range on interference control and switching tasks, but poorly on verbal working memory, inhibition, planning, and verbal fluency tasks. This unique profile of executive difficulty was largely consistent across all age groups.

To our knowledge, only two studies have looked at the role sleep plays in the association between neurocognitive deficits and preterm birth, and neither included a working memory measure. Emancipator et al. (2006) investigated the relationship between SDB and neurocognitive function in a sample of children (aged 8 -11 years)
born preterm (defined as <36 weeks in this study) and to term. Results showed that SDB was associated with deficits in cognitive functioning (e.g., receptive vocabulary, basic verbal ability, general knowledge, visuo-spatial processing and reasoning) and academic ability in children born preterm, while conversely, no association was found between SDB and the cognitive measures in the term group. Of the sleep measures used, which included polysomnography, parent-report of snoring history was the strongest predictor of cognitive deficits. This finding suggests that snoring, in addition to overall sleep quality, needs to be considered when investigating cognitive problems in children.

In a more recent study, Hagmann-von Arx and colleagues (2014) investigated whether the association between sleep and cognition differed between children (aged 6 – 10 years) born full term and very preterm. Polysomnography was used to measure sleep duration, sleep efficiency, and nocturnal awakenings, while cognitive measures assessed intelligence, arithmetic, visuo-spatial short-term memory, selective attention, and verbal short-term memory. Analyses revealed that the association between sleep and cognition was moderated by prematurity status. Better sleep efficiency in children born very preterm was related to better performance IQ, visuo-spatial short-term memory, arithmetic, and selective attention tasks, whereas there were no significant associations between sleep and cognitive outcomes in children born to term. Thus, evidence from the two studies suggests that children born preterm are highly vulnerable to the effects of poor sleep on their cognitive functioning. Perhaps surprisingly though, no study to date has examined the relationship between sleep and working memory in children born preterm.

There is, however, some evidence of a relationship between sleep and working memory in typically-developing children (Buckhalt, El-sheik, & Keller, 2007; Steenari, Vuonela, Paavonen, Carlson, Fjallberg, & Aronen, 2003). A recent meta-analysis by Astill and colleagues (2012) of 86 studies investigating sleep and cognition in healthy
children aged 5 to 12 years, found that compromised executive functioning, which included measures of working memory, inhibitory control, and cognitive flexibility, was associated with shorter sleep duration. While Astill et al. (2012) did not investigate working memory as an individual outcome measure, others have reported evidence of a direct relationship between sleep problems and poor working memory performance in children (e.g., Buckhalt et al., 2007; Steenari et al., 2003; Vriend et al., 2013). Moreover, support for a causal role of sleep comes from research by Vriend and colleagues (2013), who found that the restriction of sleep by one hour in their school-aged sample resulted in poorer performance on a range of tasks, including working memory, compared to performance when sleep was extended by an hour. In general, evidence from studies investigating performance in typically developing children suggests that poor sleep is associated with decreased working memory. Given preterm status has been linked to deficits in working memory and in sleep (Emancipator et al., 2006; Mulder et al., 2010), we aimed to clarify whether poor sleep could account for the increased working memory deficits observed in children born very preterm.

We approached the investigation of sleep and working memory in children born very preterm using Baddeley and Hitch’s multiple component view of working memory (Baddeley, 2000; Baddeley & Hitch, 1974). A number of studies have shown that independent measures of processing speed and storage capacity contribute unique variance to working memory performance in children (e.g., Bayliss, Jarrold, Gunn, & Baddeley, 2003; Jarrold, Mackett, & Hall, 2014; Magimairaj, Montgomery, Marinellie, & McCarthy, 2009). Further, Bayliss and colleagues (2003) found that the residual variance in working memory that remained following the control of variance associated with individual differences in processing speed and storage capacity was related to higher-order cognitive skills (e.g., fluid intelligence). They suggested that the residual variance potentially represented an executive component of working memory. More
recent studies (e.g., Jarrold & Bayliss, 2007; Jarrold et al., 2014) have replicated the finding of a potential executive component of working memory following the removal of variance contributed by individual differences in processing speed and storage capacity. Importantly, studies have found slowed processing speed and reduced storage capacity in children with poor sleep, although none has looked at these relationships in the context of working memory (e.g., Buckhalt et al., 2007; Calhoun et al., 2012; Sadeh, Raviv & Gruber, 2003; Vriend et al., 2013). This means that any relationships observed between sleep and working memory could potentially be explained by the impact of poor sleep on processing speed and/or storage capacity. Thus, including measures of processing speed and storage capacity is crucial in order to deconstruct the relationship between sleep and working memory in children born very preterm.

We also aimed to investigate two plausible biological mechanisms by which sleep affects children’s cognitive functioning. One possibility is that sleep-related deficits in cognitive performance are a result of reductions in attention or arousal, due to the consequences of poor sleep such as wake-state instability and daytime sleepiness (e.g., the vigilance hypothesis; Lim & Dinges, 2010). A second possibility is that certain regions of the brain, particularly the prefrontal cortex, are susceptible to neuronal injury caused by symptoms associated with SDB and that this injury results in impaired cognition (Biggs, Nixon, & Horne, 2014). In accordance with this latter theory, Beebe and Gozal (2002) argue that the dysfunction of the prefrontal cortex caused by these sleep mechanisms manifests in deficits in executive functions – a set of higher order cognitive processes used to regulate the neurocognitive abilities necessary for everyday function. Consistent with this theory, evidence from adult studies suggests poor sleep is associated with decreased performance on a number of cognitive functions mediated by the prefrontal cortex including fluid intelligence, shifting, inhibition, and working memory (Olaithé & Bucks, 2013). Thus, we investigated whether either of these two
mechanistic theories might be able to explain any potential relationship found between sleep and working memory performance in our sample.

We addressed these aims across two studies. In Study 1, we examined the verbal working memory performance of a sample of 6- and 7-year-old children born very preterm. This age range was chosen as the tripartite structure of the adult working memory model (the phonological loop, visuospatial sketchpad, and the central executive) appears to be in place by the time children reach 6 years of age (Gathercole, Pickering, Ambridge, & Wearing, 2004). Moreover, most children have ceased napping and acquired a monophasic sleep pattern by 4 to 5 years of age, which remains unchanged until the onset of adolescence (Oksar & LeBourgeios, 2006). Independent measures of verbal storage capacity and processing speed were used to assess how much of the relationship between sleep and working memory was explained by these processes. Sleep disturbance was assessed using measures of snoring and sleep quality.

To investigate whether any relationship found between sleep disturbance and working memory performance might not be better explained by simple sleepiness, secondary to sleep disturbance, we included a measure of daytime sleepiness. If no relationship remained between our sleep measures and working memory performance following the control of daytime sleepiness, this would suggest that sleep-related deficits in working memory performance are not a result of the direct effects of sleep disturbance, but rather are due to daytime sleepiness. Given the rapidly reversible nature of the cognitive deficits associated with daytime sleepiness through interventions such as naps and caffeine, and the persistent nature of cognitive deficits in children born very preterm, daytime sleepiness was not expected to be the primary mechanism underlying the impact of sleep upon working memory performance in the current study (Aylward, 2002; Dorrian, Rogers, & Dinges, 2005).
The examination of sleep-related prefrontal dysfunction as a possible mechanism underlying any relationship found between sleep and working memory performance involved three steps. The first step required our sleep measures to remain predictive of working memory performance following the control of daytime sleepiness. The second step required our sleep measures to remain predictive of working memory performance following the control of processing speed and storage capacity. Based on past research (e.g., Bayliss et al., 2003; Jarrold et al., 2007; Jarrold et al., 2014), any relationship remaining between sleep and working memory performance following the control of processing speed and storage capacity would suggest that sleep was impacting upon a potentially executive component of working memory. Given evidence from adult studies demonstrating an association between poor sleep and executive functioning (e.g., Olaite & Bucks, 2013), we expected an association between poor sleep and the executive component of working memory, thereby providing support for Beebe and Gozal’s mechanistic model (2002). The third step was to demonstrate the impact of sleep upon an independent measure of executive functioning (abstract reasoning) in a second sample of 6 to 9-year-old children born very preterm (i.e., Study 2). In this study, we introduced a comparison group of full term children, in order to explore whether the relationship between sleep and executive functioning differed between children born very preterm compared to children born full term.

Together, these studies will provide a comprehensive understanding of the impact of poor sleep upon working memory and its multiple components in children born very preterm, and insight into the mechanisms underlying the relationship between sleep and cognitive performance in school-aged children in general.

**Study 1**

Based on previous findings of associations between verbal working memory and prematurity (e.g., Aarnoudse-Moens et al., 2012), and verbal working memory
performance and sleep problems (e.g., Buckhalt et al., 2007; Vriend et al., 2013), it was expected that poor sleep quality, increased snoring, and excessive daytime sleepiness would be associated with verbal working memory deficits in our preterm sample. Sleep quality and snoring were expected to remain predictive of working memory performance after removing the unique variance of daytime sleepiness. Moreover, based on the model proposed by Beebe and Gozal (2002), sleep quality and snoring were expected to be associated with the residual working memory variance following the control of processing speed and storage capacity, suggesting a relationship between sleep and a possible executive component of working memory.

Method

Participants

In total, 89 children (36 female; $M_{age} = 6.71$ years, range: 6.07 to 7.09 years) born very preterm were recruited through the Neonatal Follow-up Program, King Edward Memorial Hospital to participate in a school-holiday activity program (Project KIDS). Median gestational age of the children was 28 weeks (IQR = 4, range: 23-32 weeks) and the median birth weight was 915 grams (IQR = 490, range: 470-2360 grams). Level of maternal education was used as a proxy for SES, as lower SES is associated with more sleep problems in children (see Buckhalt et al., 2007). Level of education was unavailable for four of the participants’ mothers (4.5%); 14 (15.7%) mothers completed up to year 10 of high school; 23 (25.8%) high school; 23 (25.8%) a college or trade certificate/diploma; 16 (18.8%) an undergraduate university degree; and 9 (10.6%) had completed a postgraduate university degree.

Tasks and Procedures

Over two consecutive days, each child was assessed on a broad cognitive test battery that included measures of children’s working memory, storage capacity, processing speed, and sleep behaviour. Psychometric testing that required individual
administration of tasks were administered in a standardised fashion one-on-one with an experienced practitioner. Some tasks, where permitted by test manuals, were administered in small group or pseudo-class settings with no more than four children at a time.

*Working memory measure*

The Digit Span Backwards subtest from the WISC-IV (Wechsler, 2003) was used to measure verbal working memory. The WISC-IV is the gold standard test of intelligence and has excellent internal reliability (Strauss, Sherman, & Spreen, 2006). In the Digit Span Backwards subtest, children are presented with sequences of digits of increasing length (minimum of 2 to a maximum of 9 digits) and asked to recall the digits in reverse order to that presented. Participants complete two trials at each length.

*Storage capacity measure*

The Digit Span Forwards subtest from the WISC-IV was used as a measure of verbal short-term storage capacity. This task requires the participant to repeat sequences of digits of increasing length (from 2 to a maximum of 9 digits, with two trials at each length) in the same order as presented. The raw scores from digit span forward and digit span backward were submitted for analysis.

*Processing speed*

The Coding and Symbol Search subtests from the WISC-IV were used as measures of processing speed. Coding and Symbol Search are paper and pencil tasks that require participants to visually scan target symbols in order to selectively discriminate symbol-matching and numbers. Both tasks were administered using standardised procedures from the manual. A combined scaled score from the two subtests was used as the measure of processing speed.
**Sleep measure**

The Sleep Disturbance Scale for Children (Bruni et al., 1996; SDSC) was completed by parents and used to measure children’s sleep patterns. The SDSC is a 26-item questionnaire which produces a total sleep score and six subscales: difficulty in initiating and maintaining sleep (DIMS), sleep breathing disorders (SDB), disorders of arousal (DA), sleep–wake transition disorders (SWTD), sleep hyperhydrosis (night sweats; SH), and disorders of excessive somnolence (DOES). Parents respond on a Likert scale ranging from 1 through to 5, with higher scores indicating poorer sleep. Only the total sleep score, disorders of excessive somnolence subscale, and the snoring item from within the sleep breathing disorders subscale were used in the current study to measure sleep quality, daytime sleepiness, and snoring respectively. The total sleep score was calculated without the DOES subscale in order to tease apart the effects of sleep quality and daytime sleepiness. The SDSC has standardised norms, and displays a strong level of internal consistency among the 26 sleep items with Bruni and colleagues (1996) reporting a Cronbach’s alpha of .79 for the control group and .71 for the sleep disordered children’s group. The present study set a Cronbach’s alpha criterion of $\alpha \geq .60$, the recommended minimum cut-off criterion to ensure a scale is reliable (Nunnally & Bernstein, 1994). Both the total sleep score ($\alpha = .61$) and DOES ($\alpha = .67$) measures met this criterion. As the proportion of missing values across the sleep measure was less than 1%, Estimation Maximisation was used to impute the missing data (Allison, 2002; Schafer & Graham, 2002).

**Results**

The descriptive statistics of the sleep and cognitive measures are shown in Table 10.
### Table 10

**Descriptive Statistics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>M</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
<th>Skew</th>
<th>Kurtosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digit Span Forwards</td>
<td>87</td>
<td>6.61</td>
<td>1.50</td>
<td>2</td>
<td>10</td>
<td>0.06</td>
<td>0.75</td>
</tr>
<tr>
<td>Digit Span Backwards</td>
<td>86</td>
<td>5.17</td>
<td>2.35</td>
<td>0</td>
<td>13</td>
<td>0.91</td>
<td>1.97</td>
</tr>
<tr>
<td>Processing Speed Index</td>
<td>86</td>
<td>93.91</td>
<td>15.60</td>
<td>59</td>
<td>123</td>
<td>-0.15</td>
<td>-0.68</td>
</tr>
<tr>
<td>DOES*</td>
<td>89</td>
<td>0.82</td>
<td>0.78</td>
<td>0.70</td>
<td>1.28</td>
<td>1.28</td>
<td>1.56</td>
</tr>
<tr>
<td>TSS*</td>
<td>89</td>
<td>32.53</td>
<td>7.75</td>
<td>22</td>
<td>60</td>
<td>1.19</td>
<td>1.35</td>
</tr>
<tr>
<td>Snoring Item*</td>
<td>89</td>
<td>2.02</td>
<td>1.21</td>
<td>1</td>
<td>5</td>
<td>1.03</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Note. DOES = disorders of excessive somnolence. The DOES variable has been log transformed. TSS = total sleep score.  
1 = data were unavailable for 2 participants; 2 = data were unavailable for 3 participants, a further 3 participants scored 0. No differences were observed in results with/without these participants so they were included in all analyses. 3 = data were unavailable for 3 participants.  
*Higher scores indicate poorer sleep.

Prior to analyses, all data were checked for deviations of normality. Scores on the DOES subscale were not normally distributed and were log transformed. To begin, a series of analyses investigated the possible influence of confounding factors. An alpha level of .05 was used in all inferential statistics and one-tailed analyses were used in the correlation analyses where directional predictions were made. Effects sizes were calculated using Cohen’s $d$ (Cohen, 1988). There were significant differences in performance between males and females on the processing speed task, $t(84) = 2.36$, $p = .020$, $d = 0.52$, with females demonstrating faster processing speed than males.

Subsequently, gender was controlled for in all analyses. A series of ANOVAs was used to investigate any effects of SES (as classified by maternal education) on sleep and cognitive outcomes. Analyses revealed significant differences between SES groups in daytime sleepiness, sleep quality, and storage capacity. Based on these differences, SES was also covaried in all subsequent analyses. Pearson bivariate correlations were then performed to investigate the relationship between age and the sleep and cognitive measures. Older children had better working memory performance, $r(86) = .22$, 

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$p = .020$, and storage capacity, $r(87) = .19, p = .039$, and less daytime sleepiness, $r(89) = -.18, p = .047$. Based on these findings, age was covaried in all analyses.

One-tailed Pearson partial correlation analyses were performed to examine the relationship between the sleep and cognitive measures whilst controlling for age, gender, and SES (Table 11). Increased parent-reported snoring was not associated with poorer performance on any of the cognitive measures, whereas greater levels of daytime sleepiness (DOES) were associated with slower processing speed, and poorer overall sleep quality (TSS) was associated with poorer working memory performance.
Table 11

Partial Bivariate Correlations (controlling for Age, Gender, and SES) between Sleep Variables and Cognitive Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>DSB</th>
<th>DSF</th>
<th>PS</th>
<th>DOES</th>
<th>TSS</th>
<th>Snoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSB</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSF</td>
<td>0.26*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS</td>
<td>0.28*</td>
<td>0.01</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOES</td>
<td>-0.17</td>
<td>-0.09</td>
<td>-0.24*</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSS</td>
<td>-0.30**</td>
<td>-0.08</td>
<td>-0.14</td>
<td>0.52**</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Snoring</td>
<td>-0.15</td>
<td>-0.17</td>
<td>-0.14</td>
<td>0.07</td>
<td>0.41**</td>
<td>1</td>
</tr>
</tbody>
</table>

Note. DSB: digit span backward; PS: processing speed index; DOES: disorders of excessive somnolence; TSS: total sleep score; * p < .05; **p < .01, one-tailed. For the sake of parsimony, only significant covariates were included in analyses. The DOES variable has been log transformed. Table 1 has N for each variable.
To investigate whether daytime sleepiness accounted for the relationship between sleep quality and working memory, a hierarchical multiple regression analysis was conducted (Table 12) with the measure of verbal working memory as the dependent variable. The covariates were entered on the first step, followed by the DOES measure on the second step, and the total sleep score on the third. The three-step model significantly accounted for 15.4% of the variance in verbal working memory performance. The total sleep score remained a significant predictor of verbal working memory performance following the control of daytime sleepiness, uniquely explaining 5.8% of variance. Reversing Steps 2 and 3 showed that daytime sleepiness contributed less than 1% of unique variance to the model, and was not a significant predictor of verbal working memory performance. Thus, after controlling for the influence of age, gender, SES, and daytime sleepiness, poor sleep quality was associated with poor verbal working memory in children born very preterm, indicating that this association is not due to the children simply being sleepy.
Table 12

Relations between Children’s Sleep Quality, Daytime Sleepiness, and Verbal Working Memory

Measures

<table>
<thead>
<tr>
<th>Predictors of Verbal Working Memory</th>
<th>B</th>
<th>CI</th>
<th>β</th>
<th>R²</th>
<th>ΔR²</th>
<th>ΔF (df)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Role of Daytime Sleepiness (N=89)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 1</td>
<td></td>
<td></td>
<td>.07</td>
<td>.07</td>
<td>1.92</td>
<td>(3, 78)</td>
</tr>
<tr>
<td>Gender</td>
<td>-0.62</td>
<td>-1.68 to 0.44</td>
<td>-.13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.97</td>
<td>-0.13 to 2.06</td>
<td>.20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SES</td>
<td>0.09</td>
<td>-0.34 to 0.51</td>
<td>.04</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
<td>.10</td>
<td>.03</td>
<td>2.38</td>
<td>(1, 77)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-0.71</td>
<td>-1.77 to 0.34</td>
<td>-.15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.81</td>
<td>-0.30 to 1.92</td>
<td>.16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SES</td>
<td>0.06</td>
<td>-0.36 to 0.49</td>
<td>.03</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOES</td>
<td>-3.0</td>
<td>-6.87 to 0.87</td>
<td>-.17</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 3</td>
<td></td>
<td>.15</td>
<td>.06</td>
<td>5.17*</td>
<td>(1, 76)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-0.66</td>
<td>-1.69 to 0.37</td>
<td>-.14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.75</td>
<td>-0.33 to 1.92</td>
<td>.15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SES</td>
<td>0.05</td>
<td>-0.36 to 0.46</td>
<td>.03</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOES</td>
<td>-0.40</td>
<td>-4.81 to 4.00</td>
<td>-.02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSS</td>
<td>-0.09*</td>
<td>-0.16 to -0.01</td>
<td>-.28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steps 2 and 3 Reversed</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
<td>.15</td>
<td>.09</td>
<td>7.74*</td>
<td>(1, 77)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-0.65</td>
<td>-1.67 to 0.36</td>
<td>-.14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.76</td>
<td>-0.30 to 1.83</td>
<td>.15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SES</td>
<td>0.05</td>
<td>-0.36 to 0.46</td>
<td>.03</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSS</td>
<td>-0.09*</td>
<td>-0.15 to -0.03</td>
<td>-.30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 3</td>
<td></td>
<td>.15</td>
<td>0</td>
<td>0.03</td>
<td>(1, 76)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-0.66</td>
<td>-1.69 to 0.37</td>
<td>-.14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.75</td>
<td>-0.33 to 1.83</td>
<td>.15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SES</td>
<td>0.05</td>
<td>-0.36 to 0.46</td>
<td>.03</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSS</td>
<td>-0.09*</td>
<td>-0.16 to -0.01</td>
<td>-.28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOES</td>
<td>-0.40</td>
<td>-4.81 to 4.00</td>
<td>-.02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Role of Processing Speed and Storage Capacity (N=86)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
<td>.21</td>
<td>.14</td>
<td>4.47**</td>
<td>(3, 75)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-0.20</td>
<td>-1.15 to 0.92</td>
<td>-.04</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.63</td>
<td>-0.34 to 1.74</td>
<td>.13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SES</td>
<td>0.01</td>
<td>-0.40 to 0.45</td>
<td>.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOES</td>
<td>-1.55</td>
<td>0.01 to 0.08</td>
<td>-.09</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSI</td>
<td>0.04*</td>
<td>0.01 to 0.08</td>
<td>.26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSF</td>
<td>0.40*</td>
<td>0.07 to 0.76</td>
<td>.26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 3</td>
<td></td>
<td>.26</td>
<td>.05</td>
<td>5.03*</td>
<td>(1, 74)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-0.17</td>
<td>-1.21 to 0.81</td>
<td>-.04</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Hierarchical multiple regression analyses were then performed to investigate whether individual differences in processing speed and storage capacity might account for the variance in verbal working memory performance shared with sleep quality (Table 12). Covariates were entered in the first step of the model (this step was identical to the previous analyses and therefore is not presented in Table 12), followed by the DOES measure, processing speed, and storage capacity on the second step, and finally the total sleep score. The addition of the DOES, processing speed, and storage capacity variables at Step 2 independently predicted 14.1% of unique variance in verbal working memory performance, and the addition of the total sleep score at Step 3 contributed a further 5.0% of unique variance to verbal working memory. Thus, the sleep measure remained predictive of verbal working memory performance following the removal of variance associated with the independent measures of processing speed and storage capacity. This indicates that there was an association between sleep and the residual variance in working memory, which potentially represents the executive component of working memory.

**Discussion**

The results from this study showed that poor sleep quality in children born very preterm is predictive of decreased verbal working memory performance, and that this relationship is not simply due to children being sleepy during the day as a consequence
of poor sleep. Despite not finding an association between snoring and working memory, our finding of a relationship between sleep quality and working memory is in agreement with previous studies (e.g., Emancipator et al., 2006; Hagmann-von Arx et al., 2014), that have also found sleep problems to be associated with poorer cognitive outcomes in children born preterm. Furthermore, consistent with previous studies with typically developing children (e.g., Alloway et al., 2006; Bayliss et al., 2003; Magimairaj et al., 2009), processing speed and storage capacity were both found to be independent predictors of verbal working performance. Children born very preterm with slowed processing speed and reduced storage capacity performed more poorly on the verbal working memory task than children born very preterm without these basic cognitive constraints. However, importantly, sleep quality remained predictive of the residual variance in verbal working memory after accounting for individual differences in processing speed and storage capacity.

The finding of an association between sleep quality and the residual variance in verbal working memory performance has implications for theories regarding the mechanisms underlying the relationship between sleep problems and children’s daytime functioning. Our findings did not support daytime sleepiness as an underlying mechanism by which cognition is adversely affected in children. This was as expected, due to research indicating that working memory deficits in children born very preterm can be longstanding (Aarnoudse-Moens et al., 2012), whereas the nature of cognitive deficits associated with daytime sleepiness are readily reversible (Beebe & Gozal, 2002). In contrast, our findings provide support for Beebe and Gozal’s model (2002), which proposes that the effect of sleep problems, such as snoring or sleep dysregulation, impacts primarily on the prefrontal cortex, and that this dysfunction manifests as executive dysfunction (Beebe & Gozal, 2002). Past research (Bayliss et al., 2003; Jarrold et al., 2007; Jarrold et al., 2014) suggests that the variance in working memory
that remains once variance associated with processing speed and storage capacity is removed, reflects the executive coordination of the individual components of working memory. Our findings, then, could be taken to indicate that poor sleep quality is associated with dysfunction in an executive component of working memory, rather than the basic storage and processing components. This is consistent with the claim that prefrontal dysfunction is the primary mechanism underlying the relationship between sleep problems and cognitive deficits. The relationship between sleep and a potential executive component of working memory was further explored in Study 2.

Study 2

To explore the association between sleep problems, birth status and the functioning of the executive system more directly, Study 2 introduced an independent measure of executive functioning to investigate whether sleep problems would differentially impact the executive functioning of children born very preterm versus children born to term. It was expected that sleep problems in children born very preterm would have a greater impact on executive functioning relative to children born to term. The rationale underlying our approach was that, as a consequence of the medical complications most commonly experienced by children born very preterm (e.g., PVL), many children within this population will have suffered insult to the neural connectivity within prefrontal circuits, particularly the frontostriatal pathways that mediate executive functioning (Duerden, Card, Lax, Donner, & Taylor, 2013; Edgin, Inder, Anderson, Hood, Clark & Woodward, 2008). Given the increased likelihood of a pre-existing insult to the prefrontal cortex in children born very preterm, if, based on Beebe and Gozal’s model, the impact of poor sleep is primarily to the prefrontal cortex, then it would be expected that the presence of sleep problems in children born very preterm would have a detrimental effect upon executive functioning, more so, than would be expected by the effects of prematurity or sleep problems alone. Recent research
suggests that not only are children with sleep problems more likely to have deficits in executive functioning than children with no sleep complaints (e.g., Astill et al., 2012), but that children born very preterm are also more likely than their full term counterparts to have executive dysfunction (Aarnoudse-Moens et al., 2009). Further, while neither included a standalone measure of executive functioning, evidence from Emancipator et al. (2006), and Hagmann-von Arx et al. (2014) suggests that the association between sleep problems and deficits in cognition is stronger in children born preterm than in children born at term. If the mechanism by which sleep is impacting on children’s cognition is through dysfunction of the prefrontal cortex, which manifests behaviourally as executive dysfunction (Beebe & Gozal, 2002), then it is reasonable to expect an interaction between sleep problems and preterm status that would result in poorer executive functioning than would be expected by the effect of prematurity or sleep problems alone.

Based on previous research (e.g., Aarnoudse-Moens et al., 2012; Astill et al., 2014), we expected that children with problematic levels of sleep would perform more poorly on the executive task than children with few or no sleep problems (irrespective of birth status). Further, given the evidence from a number of studies demonstrating increased executive difficulty in children born very preterm relative to children born to term (for a review see Aarnoudse-Moens et al., 2009), children born very preterm were expected to perform more poorly than their full term counterparts on our measure of executive functioning. Finally, based on Hagmann-von Arx et al. (2014) and Emancipator et al. (2006), we expected that sleep problems in children born very preterm would have a stronger, negative effect on executive functioning than children born to term.
**Method**

**Participants**

*Children born Very Preterm*

Participants recruited for Study 2 included 43 children (21 female; $M_{age} = 7.84 \pm 1.11$ years, range: 6.10 to 9.05 years) born very preterm. Children were recruited through the Neonatal Follow-up Program at King Edward Memorial Hospital and attended Project K.I.D.S. (35 of whom were included in the Study 1 sample; of these, 17 completed the tasks included in Studies 1 and 2 concurrently, and 18 completed the tasks over two separate Project KIDS programs). Median gestational age of the children was 27 weeks ($IQR = 4$, range: 23-32 weeks) and the median birth weight was 810 grams ($IQR = 350$; range: 455-1945 grams). Level of education was unavailable for four of the very preterm participants’ mothers (9.3%). Four (9.3%) mothers had completed up to year 10 of high school, 11 (25.6%) had completed high school, 9 (20.9%) had completed a college or trade certificate/diploma, 7 (16.3%) had completed an undergraduate university degree, and 8 (18.6%) had completed a postgraduate university degree.

*Children born to Term*

Forty-eight children born to term (26 female; $M_{age} = 7.52 \pm 1.13$ years, range: 6.03 to 9.11 years) who attended the University of Western Australia’s Project K.I.D.S. (Kid’s Intellectual Development Study) were also recruited to participate in the study. The project recruits children from approximately 42 schools located in and around the Perth metropolitan area. Median gestational age of the children born full term was 39 weeks ($IQR = 2$, range: 37-42 weeks) and the median birth weight was 3255 grams ($IQR = 866$; range: 2300-6400 grams). Level of education was unavailable for one of the term participants’ mothers (2.1%). Three (6.3%) mothers had completed up to year 10 of high school, 10 (20.8%) had completed high school, 3 (6.3%) had completed a
college or trade certificate/diploma, 21 (43.8%) had completed an undergraduate university degree, and 10 (20.8%) had completed a postgraduate university degree.

**Tasks and Procedures**

Tasks were administered in the same format as Study 1.

**Executive Functioning**

To measure executive functioning, the Matrix Reasoning subtest from the WISC-IV was used. Matrix Reasoning measures a child’s abstract reasoning and problem solving ability across four categories of nonverbal reasoning ability (pattern completion, classification, analogy, and serial reasoning), and has been associated with activation in dorsolateral and rostrolateral prefrontal cortex (Christoff et al., 2001; Kroger, Sabb, Fales, Bookheimer, Cohen, & Holyoak, 2002; Masunaga, Kawashima, Horn, Sassa & Sekiguchi, 2008). The participant is required to complete the design or matrices displayed by selecting the missing section from the choices provided. The Matrix Reasoning task has excellent (.80-.89) internal consistency. The total correct score was taken as the measure of executive function.

**Sleep measure**

Consistent with Study 1, the Sleep Disturbance Scale for Children (Bruni et al., 1996; SDSC) was used to measure children’s sleep patterns. However, as snoring was not associated with working memory performance in Study 1, this study used the total sleep score only. The total sleep score was calculated with the DOES score included in order to obtain scaled scores from the norms provided by Bruni et al. (1996). Clinical levels of sleep problems were then determined based on criteria used by Blunden et al. (2005) when administering the same sleep scale (i.e., a T-score ≥ 67). Total sleep scores were coded as either clinically elevated or non-problematic depending on where they fell with regards to the cut-off criteria. As the proportion of missing values across the
sleep measure was less than 1%, Estimation Maximisation was used to impute the missing data (Allison, 2002; Schafer & Graham, 2002).

**Results**

Table 13

*Means and Standard Deviations for Matrix Reasoning by Sleep and Birth Group*

<table>
<thead>
<tr>
<th>Sleep Type</th>
<th>Birth Type</th>
<th>N</th>
<th>Matrix Reasoning</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal sleep</td>
<td>Preterm</td>
<td>35</td>
<td></td>
<td>16.57</td>
<td>5.85</td>
</tr>
<tr>
<td></td>
<td>Full Term</td>
<td>42</td>
<td></td>
<td>20.05</td>
<td>5.00</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>77</td>
<td></td>
<td>18.47</td>
<td>5.64</td>
</tr>
<tr>
<td>Problematic sleep</td>
<td>Preterm</td>
<td>8</td>
<td></td>
<td>9.62</td>
<td>2.93</td>
</tr>
<tr>
<td></td>
<td>Full Term</td>
<td>6</td>
<td></td>
<td>19.00</td>
<td>5.69</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>14</td>
<td></td>
<td>13.64</td>
<td>6.34</td>
</tr>
</tbody>
</table>

Note. Higher scores on the executive function measure indicate better performance.

The Matrix Reasoning scores met criteria for normality. There were no group differences between children born very preterm and to term in age, \( t(89) = 1.34, p = .182 \), or gender, \( \chi^2 (1) = .26, p = .612 \). A chi square test of independence revealed significant differences in SES, \( \chi^2 (4) = 9.75, p = .045 \), with children born at term more likely to have mothers who had completed undergraduate university degrees than children born very preterm. However, there was no association between SES and Matrix Reasoning scores in the very preterm group, \( r(39) = -.11, p = .491 \), the full term group, \( r(47) = .21, p = .162 \), nor when both birth groups were combined, \( r(86) = .11, p = .327 \). Nor were there any gender differences in Matrix Reasoning scores, \( \chi^2 (23) = 15.52, p = .875 \). In contrast, age was correlated with Matrix Reasoning scores, \( r(91) = .42, p < .001 \). Consequently, of the three possible covariates, only age was added as a covariate in subsequent analyses.

The means and standard deviations for each analysis are presented in Table 13. A 2–way ANCOVA was conducted to test for the effects of sleep problems and birth
type (very preterm, term) on matrix reasoning scores. Levene’s Test of Equality of Variances was non-significant, $F(3, 87) = 2.13, p = .102$, indicating equal variance across groups. The very preterm group scored significantly lower than the term group on the Matrix Reasoning task, $F(1,86) = 26.92, p < .001, \eta^2 = .39$. The effect of sleep problems was also significant, $F(1,86) = 6.79, p = .011, \eta^2 = .10$, indicating that children with clinically significant levels of sleep problems achieved lower Matrix Reasoning scores when compared to children with non-problematic levels of sleep problems. The interaction between sleep and birth type was non-significant, but did show a trend towards significance, $F(1,86) = 3.47, p = .066, \eta^2 = .204$.

Given the trend towards significance, we explored the impact of sleep on Matrix Reasoning scores for each birth type separately. Two separate ANCOVAs were conducted with Matrix Reasoning scores as the dependent variable and sleep problems as the independent variable, whilst controlling for age. These analyses revealed no significant differences in Matrix Reasoning scores between children with or without sleep problems in the term group, $F(1,45) = 0.29, p = .59, \eta^2 = .01$. In contrast, in the very preterm group, children with sleep problems performed more poorly on the Matrix Reasoning task than children with no sleep problems, $F(1,40) = 9.49, p = .004, \eta^2 = .48$. These results, which must be interpreted with caution, suggest that the main effect of sleep problems on Matrix Reasoning was driven primarily by sleep problems in children born very preterm alone. Further, these results suggest that being born very preterm and having problematic sleep results in poorer executive functioning than prematurity or sleep problems alone.

**Discussion**

Study 2 was designed to explore the impact of sleep on the executive functioning of children born very preterm more directly. Sleep problems in children born very preterm resulted in decreased Matrix Reasoning scores relative to children...
born very preterm with no sleep problems. Accordingly our results provide support for
the suggestion from Study 1 that poor sleep is associated with poorer executive
functioning in children born very preterm. Further, our results suggest the presence of
an interaction between sleep and prematurity upon children’s executive functioning
(albeit at trend level). Consistent with Hagmann-von Arx et al. (2014) and Emancipator
et al. (2006), we found that sleep problems in children born very preterm resulted in
decreased performance on the executive measure, whereas sleep problems did not
appear to affect performance in the term group. This supports our hypothesis that
children born very preterm would be more vulnerable to sleep-related executive
difficulty than children born at term, most likely as a result of insult to the prefrontal
cortex via sleep problems and perinatal complications associated with prematurity.

General Discussion

The current studies were designed to investigate the relationship between sleep
and working memory in children born very preterm, and the mechanisms by which
sleep impacts upon children’s cognition. More specifically, we were interested in how
much of the relationship between sleep and working memory was explained by storage
capacity, processing speed, and daytime sleepiness, and whether sleep-related injury to
the prefrontal cortex, evident as decreased executive functioning, might be driving the
relationship between sleep and working memory in children born very preterm. One key
finding was that sleep quality was associated with working memory performance, above
and beyond the influence of daytime sleepiness, processing speed, and storage capacity.
A second key finding was that sleep problems adversely affected the executive
functioning of children born very preterm, but not children born to term.

The finding of an association between sleep and working memory in children
born very preterm is consistent with a number of other studies that have demonstrated
the same association in typically developing school-aged children (e.g., Buckhalt et al.,
2007; Steenari et al., 2003; Vriend et al., 2013), and extends this relationship to children born very preterm. Although Emancipator et al. (2006) and Hagmann-von Arx et al. (2014) both demonstrated that poor sleep was associated with poor performance on a number of cognitive abilities in children born preterm, neither study included a measure of working memory. The results from Study 1 suggest that poor sleep may also account for some of the working memory difficulties experienced by children born very preterm. Importantly, this is in addition to any impact of sleep upon the processing speed and storage capacity components of working memory, which in the past have been found to be adversely affected by poor sleep (e.g., Buckhalt et al., 2007; Sadeh et al., 2003). Our results indicate that the relationship between sleep and working memory cannot be explained by slower processing speed or reduced storage capacity associated with poor sleep, and instead suggests an association between sleep and a potential executive component of working memory.

Findings from Study 2 support the suggestion of an association between sleep and a potential executive component of working memory found in Study 1, in that results clearly showed a negative effect of sleep problems on the executive functioning of children born very preterm. Importantly, as no evidence of an association was found between daytime sleepiness and working memory in Study 1, when taken together, results from both studies imply that the primary mechanism by which sleep affects cognition in children born very preterm is through sleep-related insult to the prefrontal cortex. This is consistent with Beebe and Gozal’s mechanistic model (2002) of sleep-related prefrontal and executive dysfunction.

Further, this study shows that sleep problems in children born very preterm, by virtue of their prematurity, pose an additional threat to executive functioning relative to typically developing children. This makes sense from a cognitive reserve perspective, if one considers that children born very preterm are more likely to have experienced early
insult to the prefrontal regions as a result of perinatal complications (Edgin et al., 2010). This would make children born very preterm less able to compensate for sleep-related neuronal insult in and around the prefrontal cortex, when compared to children born to term. The use of neuroimaging in future studies will help to clarify any sleep-related differences in brain activity between very preterm and term children.

Another interesting finding was the failure to find an association between snoring and working memory performance in our study. This was in contrast to Emancipator and colleagues (2006), who found that snoring was the strongest predictor of cognitive performance in children born preterm. Our use of a single, subjective sleep measure may have restricted our capacity to detect an effect of snoring on cognition. Parents were not forewarned to monitor their children’s sleep so it is possible that a number of children who snored were rated as non-snorers (or vice versa). Further, it is difficult to be sure that the severity of snoring in each child was consistently judged across individual parents. To address these limitations in future studies, it is recommended parents be forewarned to the necessity of monitoring their child’s sleep in advance of testing. Moreover, parents of participants may benefit from being provided (in advance) information on what constitutes abnormal and normal sleep behaviors, in order to enable them to respond accurately to sleep items on questionnaires. Finally, future studies may want to include an objective measure of sleep (e.g., actigraphy) in conjunction with a questionnaire to obtain a more accurate picture of children’s sleep.

The central clinical implication from our study is the importance of identification and early intervention for sleep problems in children, and the importance of screening for sleep problems in children born very preterm. While the proportion of variation in working memory explained by sleep in our study is relatively modest (5.6%), this proportion is in addition to any variance shared between sleep and processing speed and storage capacity, two processes that are known to independently
contribute to children’s working memory (e.g., Bayliss et al., 2003; Jarrold et al., 2014; Magimairaj et al., 2009). Given the strong link between working memory performance and learning difficulties, even the smallest improvements in sleep may lead to improvements in academic performance, and reduce the risk of a child falling behind their classmates.

In conclusion, the results from the present study indicate that poor sleep quality is associated with poor verbal working memory in a very preterm population, and that this association is not simply due to daytime sleepiness. Multiple factors have been demonstrated to contribute to verbal working memory performance including processing speed and storage capacity, which suggests these cognitive functions need to be taken into account when assessing working memory deficits in children. Sleep problems were identified as placing additional burdens upon the executive functioning of children born very preterm relative to children born to term. Going forward, neuroimaging will assist in further investigations into the specific brain areas driving these additional burdens. Unlike prematurity, sleep problems are treatable. Results from the current study drive home the importance of preventative screening for sleep problems in a very preterm, paediatric population, which may help to detect children who are at risk of cognitive difficulties.

References


Chapter 7:

General Discussion
This thesis investigated the relationship between sleep and working memory in school-aged children. The rationale for the thesis came from research that has found poor sleep to adversely affect children’s daytime functioning, in particular, impacting on academic outcomes, producing daytime sleepiness, decreasing vigilance, increasing inattention, slowing processing speed, and decreasing executive functioning (Astill, Van der Heijden, Van IJzendoorn, & Van Someren, 2012; Beebe, 2011; Buckhalt, El-sheik, & Keller, 2007; Dewald, Meijer, Oort, Kerkhof, & Bogels, 2009). Moreover, adult studies confirm that poor sleep is associated with reduced working memory performance (e.g., Beebe, Groesz, Wells, Nichols, & McGee, 2003; Durmer & Dinges, 2005; Olaite & Bucks, 2013). Thus, the premise of this thesis was that sleep may be one of several factors that underlie individual differences in children’s working memory performance. However, to date, this has been an under-researched area, and the few results have been inconsistent. Further, within those studies investigating sleep and working memory in children, very few have been theoretically driven. As such, the operationalisation of working memory performance has been variable, with very little consideration given to the multiple components that make up working memory, or the mechanisms underlying the relationship between sleep and working memory performance in children.

Accordingly, the aim of this thesis was to examine the relationship between sleep and working memory in school-aged children, and to approach the investigation from a solid, theoretical foundation. Working memory was conceptualised based upon one of the most influential models to date, Baddeley and Hitch’s working memory model (Baddeley, 2000; Baddeley & Hitch, 1974), which proposes the fractionation of working memory into separate verbal and visuospatial storage systems, a domain-general central executive, and an episodic buffer. Research based on this model has shown that both processing speed and storage capacity contribute unique variance to
working memory performance and should be accounted for in working memory investigations (Bayliss, Jarrold, Gunn, & Baddeley, 2003; Jarrold, Mackett, & Hall, 2014; Magimairaj, Montgomery, Marinellie, & McCarthy, 2009). Moreover, research by Bayliss et al. (2003) has demonstrated the existence of a third component, consisting of the residual variance following the removal of variance from processing speed and storage capacity. This third component is thought to reflect the central executive responsible for the coordination of the processing and storage components of working memory (Bayliss et al., 2003; Jarrold et al., 2014). As such, measures of processing speed and storage capacity were included in the current research in order to tease apart the contribution to performance of the three working memory components (including the residual variance thought to reflect the central executive). Measures of verbal and spatial short-term and working memory were also included in the current research, based on research that has confirmed the delineation of the verbal and spatial working memory components (e.g., Alloway, Gathercole & Pickering, 2006; Jarvis & Gathercole, 2003; Steenari, Vuontela, Paavonen, Carlson, Fjallberg, & Aronen, 2003).

A second aim of this thesis was to investigate the mechanisms by which sleep impacts upon children’s working memory and cognition in general. Two main classes of theories relating to the mechanisms underlying sleep and cognition were investigated. The first group of theories (e.g., Dorian, Rogers, & Dinges, 2005; Durmer & Dinges, 2005; Williams, Lubin, & Goodnow, 1959) is based on the vigilance hypothesis, which proposes that sleep-related cognitive difficulty is due to the consequences of poor sleep (such as sleep-wake instability and daytime sleepiness) negatively impacting on children’s levels of alertness and attention. The second group of theories (e.g., Beebe & Gozal, 2002; Harrison & Horne, 1998, 2000) is based on the sleep-based neuropsychological perspective, which proposes that sleep-related neuronal injury,
occurring primarily in the prefrontal cortex, results in impaired executive functioning and, consequently, sleep-related cognitive difficulty.

The two aims of the thesis were investigated across three studies investigating performance in three, separate populations of school-aged children: typically developing children; children with neurological conditions; and, children born very preterm. Two clinical populations of children (children born very preterm and children with neurological conditions) were included in our investigations, as many children from clinical groups (e.g., autism, intellectual disability) have been found to have greater variability in sleep disturbance and cognitive performance, relative to children from non-clinical populations. Thus, children born very preterm and children with neurological conditions provide a unique opportunity to study the sleep and working memory relationship, which would not be obtained simply by investigating the relationship in typically developing children alone. Furthermore, such investigations offer insight into a potentially modifiable cause of cognitive burden in vulnerable populations such as the two clinical populations of children included in the current thesis.

In this chapter, the main findings of each empirical study conducted as part of this thesis are reviewed in turn. Following this, a discussion is provided of the theoretical implications of the findings, in terms of the cognitive structure of working memory and the proposed mechanisms by which sleep impacts cognition. The chapter ends with a discussion of the clinical implications from the three studies, limitations of the research, and suggestions for future directions.
Review of Key Findings

Study 1

The first study (Chapter 4) investigated sleep and working memory performance in typically developing, school-aged children. The rationale behind Study 1 was that there is an association between sleep and working memory in adults (e.g., Beebe et al. 2003; Olathe & Bucks, 2013) and, while inconsistent, there is some evidence of an association in children (e.g., Buckhalt et al., 2007; Steenari et al., 2003; Vriend, Davidson, Corkum, Rusak, Chambers, & McLaughlin, 2013). Further, results from a recent meta-analysis by Astill et al. (2012) demonstrated an association between shorter sleep duration and working memory when measured alongside inhibitory control and cognitive flexibility. While not measured independently, the relationship demonstrated in the Astill et al. study (2012), in addition to the association demonstrated in adults, gave cause to investigate, in depth, the relationship between sleep and working memory performance in school-aged children. Taking a theoretical approach, it was proposed that the use of multiple measures of working memory and sleep might help to unravel the mixed evidence from previous studies.

Study 1 included measures of verbal and nonverbal working memory, verbal and nonverbal storage capacity, and processing speed. Similarly, a number of measures were used to index poor sleep, reflecting the severity of disorders of arousal, snoring, daytime sleepiness, and poor sleep quality. Daytime sleepiness was included specifically to test the vigilance hypothesis, while the residual variance in working memory performance remaining after removing variance attributed to processing speed, storage capacity, and daytime sleepiness, was used to investigate the sleep-based neuropsychological perspective. In contrast to previous research (e.g., Buckhalt et al., 2007; Steenari et al., 2003), no relationship was found between any of the sleep and working memory measures. It was noted that the failure to find an association may have been due to a
lack of variability in sleep parameters, with minimal sleep problems reported in the Study sample.

**Study 2**

As noted above, the majority of parents in Study 1 reported few sleep problems in their children. To overcome this limitation, Study 2 investigated the sleep and working memory relationship in school-aged children presenting for neuropsychological assessment with known or suspected brain injury resulting from trauma, disease or genetic conditions. These children have a number of diagnosed, neurological conditions including epilepsy, cerebral palsy, and acquired brain injury. The rationale behind choosing to study children with neurological conditions came from two key findings; a) these children are at increased risk of sleep problems relative to typically developing children (Beebe, 2012; Dorris, Scott, Zuberi, Gibson, & Espie, 2008; Kothare & Kotagal, 2011), and b) these children are also at increased risk of working memory problems (Conklin, Salorio, & Slomine, 2008; Jenks, de Moor, & van Lieshout, 2009; Longo, Kerr, & Smith, 2013). This study took a novel, transdiagnostic approach, treating sleep as a process that could explain the increased deficits evident in working memory performance in children with neurological conditions.

As in Study 1, we assessed verbal and nonverbal working memory and storage capacity, processing speed, snoring, sleep quality, and daytime sleepiness. Results demonstrated the clinical utility in taking a transdiagnostic approach to the investigation of sleep and working memory in children with neurological conditions, in that poorer sleep quality was significantly associated with verbal working memory performance within this population of children. No relationship was observed between spatial working memory and sleep quality. This pattern of findings was consistent with those of a recent paper by Lau et al. (2015), who found that children with obstructive sleep apnoea (OSA) had significantly poorer verbal working memory performance compared
to children with no OSA, whereas no such differences were noted on spatial working memory tasks. In the current research, a regression analysis revealed that sleep quality remained predictive of verbal working memory performance following the control of processing speed, and storage capacity. In line with previous research (Bayliss et al., 2003; Jarrold et al., 2014), this finding suggested that sleep was associated with the central executive component of working memory. Interestingly, no associations were demonstrated between snoring and any of the cognitive measures. While these results contradict those of previous studies (e.g., Blunden & Beebe, 2006; Bourke et al., 2011; Emancipator et al., 2006), they are in line with the studies of Biggs and colleagues (2011) and Beebe and colleagues (2004).

Despite recruiting children with a much broader range of sleep difficulties, Study 2 also failed to find an association between daytime sleepiness and working memory in a sample of children referred for neurological investigation. This is inconsistent with the vigilance hypothesis, in that daytime sleepiness secondary to disturbed sleep could not account for the association between poor sleep quality and decreased working memory. Further, support for the sleep-based neuropsychological perspective was mixed. While the relationship between poor sleep quality and the residual variance in verbal working memory suggested the mechanism underlying the relationship could be sleep-related prefrontal dysfunction, the failure to find a parallel association between disrupted sleep and spatial working memory suggests that the nature of the deficits may be specific to the verbal domain. The sleep-based neuropsychological perspective proposes global prefrontal dysfunction, whereas the results from Study 2 suggest the impact of poor sleep may be limited to certain areas of the prefrontal cortex: a point that will be discussed in the theoretical implications section.
While investigating the prevalence of sleep problems, it was noted that a large proportion of children in the birth complications group were reported to have high estimates of problematic sleep, particularly habitual snoring. Importantly, one third of this group was made up of children who were born preterm. To that end, Study 3 focused on children born very preterm.

**Study 3**

Following on from Study 2, Study 3 examined the relationship between sleep and working memory in children born very preterm. Recent work by Hagmann et al. (2014) demonstrated evidence of an association between poor sleep and decreased cognitive performance in children born very preterm, although no measure of working memory was included in the study. Given children born very preterm are at increased risk of sleep problems and working memory deficits, relative to children born to term (Aarnoudse-Moens, Smidts, Oosterlaan, Duivenvoorden, & Weisglas-Kuperus, 2009; Rosen et al., 2003), this population of children again provided a unique opportunity further to explore the sleep and working memory relationship.

Study 3 differed slightly in methodology. The study was split into two parts. The first part of Study 3 was similar to Studies 1 and 2, in that we assessed sleep quality, daytime sleepiness, and snoring, in addition to verbal working memory, verbal storage capacity, and processing speed. Consistent with Study 2, poorer sleep quality was associated with poorer verbal working memory performance above and beyond the influence of processing speed, storage capacity, and daytime sleepiness. Again, this was taken as support for the sleep-based neuropsychological perspective. Further, daytime sleepiness was not associated with any of the working memory measures, which is inconsistent with the vigilance hypothesis. Finally, as in Study 2, snoring was not associated with working memory performance.
The second part of the study investigated the association between sleep and an executive component of working memory more directly, by including a measure of matrix reasoning. A comparison group of children born to term was included to investigate whether there were group (very preterm versus term) differences in the impact of poor sleep upon children’s executive functioning. If the sleep-based neuropsychological perspective is correct, that sleep-related neuronal damage occurs primarily to the prefrontal cortex, then it would be expected that being born very preterm and having disturbed sleep would result in greater decrements to executive functioning than the effects of prematurity or poor sleep alone. It was proposed that many children born very preterm might have pre-existing vulnerability to prefrontal disruption and, based on the sleep-based neuropsychological perspective, this vulnerability when coupled with sleep problems, would exacerbate pre-existing executive functioning difficulties.

Results showed an effect of problematic sleep on children’s matrix reasoning scores regardless of birth group, in that poor sleepers had decreased performance compared to non-problematic sleepers. An effect of prematurity on matrix reasoning scores was also found, in that children born very preterm performed less well than children born to term. Contrary to prediction, however, the interaction between prematurity and poor sleep on matrix reasoning scores was not significant, although the interaction was at trend level. Given the small numbers of children in each group with problematic sleep, the failure to find a significant interaction may have been due to insufficient power (a point considered in the limitations section). As such, separate analyses were run by birth group. While results must be interpreted with caution, sleep problems in children born very preterm adversely impacted on matrix reasoning scores, whereas matrix reasoning scores in children born to term appeared unaffected by poor sleep. Thus, the finding from the main analysis of an effect of poor sleep upon
performance regardless of birth group appears to have been driven by the effect of poor sleep in children born very preterm alone. Results confirmed the relationship demonstrated between sleep and an executive component of working memory in the first part of Study 3, and the hypothesis that the addition of sleep problems in children born very preterm would have detrimental effects upon their executive functioning relative to children born to term. Results also added further support to the sleep-based neuropsychological perspective.

**Theoretical Implications of the Main Findings**

**Sleep and Working Memory**

Results from past research, investigating the relationships between sleep and working memory in typically developing school-aged children have been mixed, with some studies finding evidence for a relationship (e.g., Buckhalt et al., 2007; Steenari et al., 2003), and others finding no evidence (Sadeh, Gruber, & Raviv, 2003; Vriend et al., 2012). Consistent with Sadeh et al. (2003) and Vriend et al. (2012), no relationship was found between sleep and working memory in typically developing children in Study 1. Nor were any relationships found between sleep and the subcomponents of working memory - processing speed and storage capacity. This would suggest that working memory is not affected by sleep disturbance in typically developing children. Nonetheless, much like the Sadeh et al. (2003) study, a disproportionately large number of typically developing children (70%) were reported in Study 1 as coming from the top two tiers of our socioeconomic status (SES) scale (mothers with undergraduate or postgraduate university degrees). This may have limited the ability to detect a relationship for two reasons, the first being that SES has been found to moderate the effects of poor sleep upon children’s cognitive performance (Buckhalt et al., 2007). This would suggest that working memory performance may not be affected by sleep disturbance in typically developing children from high SES groups, which would explain the findings from
Study 1. The second reason that having a disproportionately large number of typically developing children from high SES groups may have limited our ability to detect an association, is that low SES is associated with increased sleep problems (Anderson, Storfer-Isser, Taylor, Rosen, & Redline, 2009). Indeed, there was very little variability within the sleep parameters in Study 1, with the majority of parents reporting little or no sleep disturbance in their children. Past studies (Buckhalt et al., 2007; Steenari et al., 2003) that have made a conscious effort to include typically developing children from all SES backgrounds, have found evidence of significant associations between sleep and working memory. Greater variability in SES background in the Study 1 sample may have permitted the detection of an association between sleep and working memory performance in typically developing children.

An association between poor sleep quality and verbal working memory performance was, however, demonstrated in the current research in children with neurological conditions and children born very preterm. Results across Studies 2 and 3 suggest an increased vulnerability to the adverse effects of sleep upon working memory performance in these two clinical populations of children, relative to typically developing children. Results from the current research are consistent with a number of studies that have examined the impact of poor sleep on cognition in children with neurological conditions and children born very preterm (e.g., Emancipator et al., 2006; Hagmann-von Arx et al., 2014; Sawyer et al., 2009; Zambrano-Sanchez, Martinez-Cortes, Dehesa-Moreno, Rio-Carlos, & Poblano, 2013), and extend these findings to working memory more specifically. Given that studies have demonstrated these two populations of children to be at increased risk of working memory difficulties when compared to typically developing children (Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, & Oosterlaan, 2009; Doris, Scott, Zuberi, Gibson, & Espie, 2008; Kothare & Kotagal, 2011), results from the current research suggest that sleep quality may
account for a small proportion of the working memory difficulties experienced by these children. It is acknowledged that the proportion of variance accounted for by sleep quality was small in both Study 2 and 3. However, given that verbal working memory performance is strongly associated with children’s reading decoding, reading comprehension, and written language - all skills that are essential in a learning environment - even a small improvement in a child’s ability to store or manipulate information following the treatment of sleep problems may result in improvements in one or more of these skills and reduce the risk of academic underachievement in these two vulnerable populations of children (Dehn, 2011; Kuriyama, Mishima, Suzuki, Aritake, & Uchiyama, 2008).

The use of multiple measures enabled an investigation into which component of working memory was associated with poor sleep. Studies 2 and 3 demonstrated that processing speed and storage capacity contributed unique variance to working memory performance, and that the residual variance that remained following the control of processing speed and storage capacity reflected more than just error variance. Indeed, of the three working memory components, sleep was found to be significantly associated only with the residual variance, with no significant associations observed between sleep and processing speed or storage capacity. Sleep was also associated with a direct measure of executive functioning – matrix reasoning – in Study 3, providing converging evidence that the relationship between working memory and sleep reflected the impact of sleep on the central executive component of working memory. The current research was novel in its approach to the investigation of sleep and working memory, in that no other study has broken down working memory into its three component abilities when investigating the impact of sleep. A recent study by Lau et al. (2015) purported to isolate the basic storage component from the central executive within each domain of working memory. However, while independent measures of storage capacity and the
central executive were included in the Lau et al. (2015) study, the researchers failed to statistically control for storage capacity when examining the difference in working memory performance between children with and without obstructive sleep apnoea. Thus, they did not account for the unique variance contributed by storage capacity to working memory performance and, therefore, failed to isolate the central executive. Results from the current research demonstrate the importance of deconstructing working memory into its subcomponents when investigating the impact of sleep, given sleep quality was only found to impact upon the central executive.

While it is acknowledged that interpretation of the current results is limited by the use of subjective measures of sleep (which will be discussed in the limitations section), and that typically developing children did not have sleep problems which limited the interpretation of results to two clinical populations only, it should be noted that results from Study 2 are not consistent with a domain general central executive, as was proposed in Baddeley and Hitch’s model of working memory (1974). If the central executive is conceptualised as a unitary structure, then (assuming the measures were equally sensitive) sleep would be expected to be associated with an executive component of both verbal and spatial working memory. In the current study, however, an association was found between sleep and an executive component of verbal working memory only. The finding of a dissociation at an executive level between verbal and spatial working memory stands in contrast with the large body of research which posits separate pools of resources at the level of the phonological loop and visuospatial sketchpad only (e.g., Bayliss et al., 2003; Alloway et al., 2006). Nonetheless, our findings are consistent with studies that have demonstrated that the separability of verbal and spatial working memory goes beyond the two slave systems, with each domain thought to involve both manipulation and maintenance (e.g., Friedman & Miyake, 2000; Jarvis & Gathercole, 2003; Shah & Miyake, 1996). While the current
research did not specifically include a factor analysis to explore the separability of the verbal and spatial working memory components, results from Study 2 are consistent with the idea that a distinction should be made between verbal and spatial working memory beyond the slave systems. Clearly, as this distinction was only made in one out of three of the studies in the current research, more studies investigating the distinction between verbal and spatial working memory beyond the slave systems is needed.

**Mechanisms Underlying the Relationship between Sleep and Working Memory**

One aim of the current research was to investigate the mechanisms underlying the relationship between sleep and working memory. To that end, daytime sleepiness was included in each study to investigate the vigilance hypothesis. The vigilance hypothesis proposes that alertness and attention, considered key to intact cognition, are severely impacted by the consequences of poor sleep (e.g., daytime sleepiness), which results in compromised cognitive performance (Kilgore, 2010). In all three studies, daytime sleepiness did not predict working memory performance, nor did the removal of variance contributed by daytime sleepiness affect the significant association between sleep quality and working memory. Thus the failure to find an association between daytime sleepiness and children’s working memory is inconsistent with the vigilance hypothesis. It is noted that daytime sleepiness was retained in all analyses despite not being predictive of working memory, based on research that notes it is good practice to retain predictors in the model that were set a priori, particularly if the predictors are central to the hypotheses of the study (Babyak, 2004).

Another finding that was inconsistent with the vigilance hypothesis was the lack of association between daytime sleepiness and processing speed and storage capacity. The combination of reduced processing speed and storage capacity is thought to reflect attentional capacity deficits (Verstraeten, Cluydts, Pevernagie, & Hoffman, 2004). Given only one association was found between daytime sleepiness and processing speed
(in Study 3), findings from the current research suggest that cognitive performance (e.g., working memory) may not be as sensitive to the effects of daytime sleepiness as past research suggests (e.g., Fallone, Owens, & Dean, 2002). Further, sleep quality remained predictive of working memory following the control of processing speed in Study 3, suggesting slowed processing speed (or reduced attention) cannot fully account for reduced working memory performance in children born very preterm.

Nevertheless, results from the current study only show that poor working memory performance is not a consequence of daytime sleepiness impacting upon children’s attention and alertness. Due to there being other consequences of poor sleep that may impact upon alertness and attention, such as wake-state instability and lapses caused by micro sleeps, both of which we did not specifically test for, we cannot rule out decreased attention and alertness as possible mechanisms underlying children’s sleep and cognition. To address this going forward, additional measures of the consequences of poor sleep should be included when investigating sleep and cognition. This will be discussed in the future directions section.

Results from the current research do, however, provide some support for the sleep-based neuropsychological perspective. The sleep-based neuropsychological perspective proposes that sleep-related injury to certain brain regions, primarily the prefrontal cortex, results in prefrontal dysfunction as evidenced by executive difficulties (Harrison & Horne, 2000). Results from Studies 2 and 3 strongly suggest that it is, indeed, a breakdown in an executive requirement, and not in processing or storage, driving the relationship between poor sleep quality and working memory difficulties. Thus, the direct association found between sleep quality (as opposed to daytime sleepiness) and an executive component of working memory, suggests that the mechanism underlying the association between sleep and verbal working memory is sleep-related injury to the prefrontal cortex resulting in executive function difficulties.
This makes sense when one considers that the prefrontal cortex is one of the first brain regions to be adversely affected by sleep deprivation (Drummond, Gillian, & Brown, 2001; Drummond, Brown, Gillian, Stricker, Wong, & Buxton, 2000). Further, adult studies have found that recovery sleep following sleep deprivation only results in partial recovery of frontal lobe activity (Wu et al., 2006), which is consistent with the pervasive nature of sleep-related cognitive deficits seen in children born very preterm and children with neurological conditions.

Sleep-related injury to the prefrontal cortex may explain why a relationship between sleep and working memory was only demonstrated in the two clinical populations in Studies 2 and 3, and not typically developing children. When compared to typically developing children, children born very preterm and children with neurological conditions are at an increased risk of exposure to early cerebral insults (Edgin, Inder, Anderson, Hood, Clark & Woodward, 2008; Jan et al., 2007). If poor sleep quality is then impacting upon the prefrontal cortex and affecting cognition, one might expect these children to be less able to compensate for the additional burdens placed by poor sleep upon these brain regions, relative to typically developing children. Accordingly, sleep-related cognitive difficulties would be expected to be more prominent in children born very preterm and children with neurological conditions than in typically developing children. However, to the best of the current researcher’s knowledge, no study to date has investigated the relationship between structural brain abnormalities and cognition, in relation to the consequences of sleep problems in children.

It is noted, however, that support for the sleep-based neuropsychological perspective in the current research is not unqualified. Study 2 revealed that verbal, and not spatial, working memory performance is predicted by sleep quality. More importantly, given sleep quality was not associated with storage capacity or processing
speed, this dissociation was shown to be beyond the domain-specific storage components of working memory and at an executive level. This dissociation brings into question the generality of the sleep-based neuropsychological perspective, as our results argue against sleep-related, global, prefrontal dysfunction. Rather, the findings from the current research suggest that specific areas or connections within the prefrontal cortex that mediate verbal (as opposed to spatial) executive functions may be most vulnerable to sleep difficulties. This argument is based on a large body of neuroimaging research in children, which has demonstrated the asymmetrical organisation of verbal and spatial working memory, with performance on verbal working memory tasks associated with increased left hemisphere activation and spatial with right (for a review see O’Hare, Lu, Houston, Bookheimer, Sowell, 2008; Thomason, Race, Burrows, Whitfield-Gabrieli, Glover, & Gabrieli, 2009). More specifically, studies have demonstrated that children’s performance during verbal working memory tasks results in increased activation predominantly in the left ventrolateral and dorsolateral prefrontal and parietal cortices, in contrast to spatial tasks, which show increased activation predominantly in the right dorsolateral prefrontal and parietal cortices (O’Hare et al., 2008; Thomas et al. 1999; Thomason et al., 2009; van den Bosch et al., 2014).

The dissociation between verbal and spatial working memory demonstrated in the current research suggests that certain neural substrates within the prefrontal cortex are more vulnerable to the adverse effects of sleep than others, resulting in differential performance across executive functions. Going forward, neuroimaging data are needed to confirm the neural underpinnings of the impact of sleep upon children’s working memory (and cognition in general). In adults, functional magnetic resonance imaging (fMRI) studies have demonstrated that total sleep deprivation can alter task-related activation (relative to normal sleep) in the frontal and parietal lobes during visuo-spatial working memory tasks (e.g., Chee & Choo, 2004; Choo, Lee, Venkatraman, Sheu,
Chee, 2005). To the best of the current researcher’s knowledge, no study to date has compared task-related brain activation during both verbal and spatial working memory performance following sleep deprivation, and only one fMRI study has investigated task-related activation following sleep restriction in a paediatric sample. Beebe et al. (2009) reported preliminary fMRI findings during a visuo-spatial working memory task in a small sample of adolescents (n=6; mean age = 15.3 ± 0.7). Following chronic sleep restriction (1 week of 6.5 hours per night of bed time), participants in the Beebe et al. (2009) study maintained their performance on an n-back task relative to when they were well rested (1 week of 10 hours per night of bed time). However, it was noted that participant’s neural activation differed across the two sleep conditions, in that fMRI data showed greater activation of the “task positive” network (which includes portions of the prefrontal cortex and posterior parietal lobes) and deactivation in the “task negative” network (which includes the medial frontal lobes and posterior cingulate) after chronic sleep restriction relative to performance when participants were well rested. That is, following sleep deprivation, to maintain performance across the two sleep conditions, regions that were normally activated when well-rested showed heightened activation, and regions that were normally suppressed when well-rested showed heightened deactivation. Beebe et al. (2009) concluded that the altered brain activation reflected a compensatory cerebral response elicited during sleep restriction that may have helped to preserve working memory performance. The findings from the Beebe et al. (2009) study suggest that fMRI could be a useful tool in helping to uncover any differences in the neural underpinnings of the impact of sleep upon verbal and spatial working memory performance in children with neurological conditions.

One possible explanation as to why neural substrates mediating verbal working memory/ executive functions may be more vulnerable to sleep disturbance is that differences in the developmental trajectories of the two hemispheres may leave one
hemisphere more vulnerable to insult than the other. While studies mapping brain
development in children are quite rare, volume asymmetry has been noted in children
and adolescents (aged 4 to 18 years), with slightly higher volumes of white matter
reported in the right hemisphere relative to the left (Giedd et al., 1996; Matsuzawa et.,
2001). In an early, influential model, Geschwind and Galaburda (1986) proposed that
this delayed development in the left hemisphere leaves it more vulnerable to
developmental insult when compared to the right hemisphere. Given it is highly
probable that children with neurological conditions suffered early neurological insult,
increased vulnerability in the left hemisphere would help explain why poor sleep
impacts upon verbal rather than spatial working memory, as the two domains are
thought to predominately activate the left and right hemispheres respectively.

An alternative explanation is that our spatial working memory measure did not
tap an executive ability, and that there is an association between sleep and spatial
working memory, but it was not detected using the backwards spatial span task. While
this is a possibility, previous studies using a similar spatial working memory measure
have shown backwards spatial span performance to be predictive of performance on
other executive tasks (e.g., Chey, Lee, Kim, Kwon, & Shin, 2002; Serova, 2007). Given
that research suggests that visuospatial working memory may be more closely related to
executive functioning than verbal working memory (Miyake, Friedman, Rettinger,
Shah, & Hegarty, 2001), the dissociation found in Study 2 seems unlikely to be due to
the spatial working memory task not tapping an executive ability, and more likely to be
a result of the selective effects of poor sleep as argued previously. Importantly, previous
studies have hinted at a similar dissociation between verbal and spatial working memory
when investigating the impact of poor sleep in children. For example, Lau et al. (2015)
failed to find a relationship between obstructive sleep apnoea and children’s
performance on several visuospatial working memory tasks (including a backwards
spatial span task and a visuospatial 2-back task), despite finding a significant relationship in verbal working memory performance. Further evidence comes from Steenari et al. (2003), who demonstrated stronger relationships between children’s sleep and audiospatial working memory (as measured by an audiospatial n-back task) relative to visuospatial working memory. While Steenari et al. (2003) did not include a measure of verbal working memory, the study still demonstrates the dissociation of the impact of sleep on spatial and non-spatial working memory. Thus, there appears to be some support in the literature for a dissociation of the impact of sleep upon children’s working memory performance.

Study 3 provided further support for the sleep-based neuropsychological perspective by demonstrating an effect of sleep on children’s abstract reasoning, an ability known to tap fluid intelligence (Tranel, Manzel, & Anderson, 2002). A potential difficulty in interpreting the results from Study 3 is our use of a nonverbal measure of abstract reasoning. At first sight, the finding of a significant effect of sleep upon a nonverbal measure of abstract reasoning (matrix reasoning) appears to argue against our proposal that verbal working memory/executive skills are more vulnerable to poor sleep than spatial, particularly as spatial abstract reasoning has been found to be a strong predictor of performance on matrix reasoning tasks (Dugbartey, Sanchez, Rosemaub, Mahurin, Davis, & Townes, 1999). More importantly, performance on both verbal and spatial working memory tasks has been found to predict fluid intelligence in children and, much like working memory, the performance of adults on tasks measuring fluid intelligence demonstrates increased activation predominantly in the lateral prefrontal and parietal cortices (Gray, Chabris, & Braver, 2003; Kane & Engle, 2002). Thus, it is logical that performance on a nonverbal measure of fluid intelligence would recruit the same neural substrates as those during performance on the spatial working memory task, and that similar effects of sleep on performance on the two tasks should be
evident. However, evidence suggests that performance on matrix reasoning tasks is susceptible to mediation by verbal reasoning skills (Golden, Espe-Pfeiffer, & Wachsler-Felder, 2006). For example, results from Dugbartey et al. (1999) demonstrated significant associations between performance on a matrix reasoning task and two verbal measures of executive functioning (verbal fluency and verbal abstract reasoning) in a sample of English and non-English speaking adults. Dugbartey et al. (1999) noted that their findings suggested a strong verbal mediation component of performance on the matrix reasoning task and argued that it may be misleading to call matrix reasoning a nonverbal measure. Other studies have also shown that specific subsets of matrix reasoning tasks require verbal-analytic processes (e.g., Deshon, Chan, Weissbein, 1995; Kilbourne, 2011; Welsh, 1987). While we are unable to confirm whether children in Study 3 were using verbal reasoning during the matrix reasoning task, this would explain the discrepancy between Studies 2 and 3, and support our argument of a specific prefrontal region that mediates verbal executive functions being impacted by sleep.

While results from the current research provide some support for the hypothesis that sleep-related injury impacts upon regions within the prefrontal cortex, the question remains as to which aspect of sleep disturbance is the mechanism of injury. Despite many models proposing an association between prefrontal dysfunction and disordered sleep (e.g., Dahl, 1996; Harrison & Horne, 2000), Beebe and Gozal’s heuristic model (2002) was the first to propose specific mechanisms underlying prefrontal dysfunction, and to date, remains one of the most influential. Beebe and Gozal (2002) propose that the core biological features of obstructive sleep apnoea (sleep disruption, hypoxemia and hypercarbia) disrupt the restorative features of sleep and/or disrupt cellular homeostasis in particular regions of the brain, which leads to dysfunction in the prefrontal cortex. The extent to which each mechanism is necessary or sufficient to impact upon prefrontal functioning remains unclear, as acknowledged by Beebe and...
Gozal (2002). In a review of the contribution of intermittent hypoxia, sleep deprivation, and sleep disruption to daytime performance deficits in children, Blunden and Beebe (2006) noted that results from previous studies suggest that each of these mechanisms can occur in isolation, and that each may be independently sufficient to cause daytime effects in vulnerable children. Results from the current research appear inconsistent with hypoxia and hypercarbia as mechanisms of injury, given that the sleep quality measure, which was the sum of a range of mostly non-respiratory sleep disorders, was the only sleep measure included in the current research (as opposed to snoring or daytime sleepiness) associated with working memory. That being said, however, having not included a specific measure of hypoxia and hypercarbia, we cannot rule out the influence of these mechanisms in the effects of poor sleep quality upon working memory in the current research.

Aside from hypoxia and hypercarbia, the second mechanism in Beebe and Gozal’s model (2002) is sleep fragmentation (also referred to as sleep disruption). Sleep fragmentation is the combination of the number of arousals (or awakenings) during sleep and the duration of wakefulness after sleep onset (Sadeh, Gruber, & Raviv, 2002). Sleep fragmentation occurs not only in non-respiratory sleep disorders such as bruxism and periodic limb disorder (e.g., Crabtree, Ivaneenko, O’Brien, & Gozal, 2003; Herrera, Valencia, Grant, Metroka, Chialastri, & Kothare, 2006), but also in typically developing children with no diagnosed sleep disorders (Sadeh, Raviv, & Gruber, 2000). It is highly likely that a large percentage of children in Studies 2 and 3 experienced, at minimum, a moderate level of sleep fragmentation during each night, given 34% and 20% of parents in Study 2 and Study 3 respectively, reported clinically elevated levels (T-score ≥ 67) of sleep problems in their children. As such, sleep fragmentation may be a possible mechanism mediating the effect of sleep problems upon prefrontal function in the two clinical populations of children. Interestingly, research suggests that sleep fragmentation
may trigger similar cellular and systemic damage implicated in the daytime deficits associated with intermittent hypoxia (e.g., increased oxidized stress, inflammatory cytokine production), although studies investigating these cellular and systemic mechanisms have been limited to adult and animal populations, and are yet to be translated to children (Beebe, 2005; Blunden & Beebe, 2006).

It is important to note that Beebe and Gozal’s model (2002) was updated by Beebe in 2005, to elaborate upon multiple factors that affect neurobehavioural functioning in individuals with obstructive sleep apnoea, that were not originally outlined in the earlier model. The model introduced task-relevant demands to account for deficits in neurobehavioural functioning independent of sleep, which are specific to some tasks and not others (e.g., assessment timing, skills being assessed, and environmental support provided). The model was also updated to incorporate ‘direct effects’ to account for individual and environmental factors that impact neurobehavioural functioning but are unrelated to obstructive sleep apnoea (e.g., genetic endowment, prior experience, sociodemographic factors). Finally, Beebe and Gozal’s model (2002) was modified to include risk and protective factors that affect the nature and severity of pathophysiological events associated with obstructive sleep apnoea that lead to neurobehavioural deficits. These risk and resilience factors included age/development, sociodemographic factors, sex, cognitive brain reserve, duration of disease and comorbidities. While obstructive sleep apnoea was not investigated specifically, many of the factors outlined in Beebe and Gozal’s updated model (2005) are relevant to the current research, and have been considered throughout the thesis (e.g., age, sex, sociodemographic factors, cognitive reserve). One area relevant to the current research that has not been discussed is task-specific factors. These factors are relevant, given that the different sources of data used in the three studies (e.g., archival, Project KIDS) meant that factors such as assessment timing and the environmental
support provided could not be fully controlled. Ideally, future studies will want to ensure assessment timing and the testing environment remains the same for every participant within each study.

**Clinical Implications of the Main Findings**

The finding that sleep problems in school-aged children impact upon working memory performance, underscores the importance of educating parents on the importance of sleep and the potential consequences poor sleep can have on children’s daytime functioning. Education on what constitutes good sleep hygiene can come from simple pamphlets passed on through teachers or health practitioners. Parents may not be aware that implementing simple strategies, such as limiting the use of electronic devices before bed, may help to reduce some of the behavioural sleep problems common in children. Similarly, results from the current research highlight the importance of health practitioners screening for sleep problems in children, and for working memory problems in children with sleep problems. Early identification of sleep and/or working memory problems in school-aged children would facilitate early intervention with the aim of reducing or preventing secondary problems such as learning difficulties and academic under achievement.

A novel aspect of the current research was the demonstration of the clinical utility in taking a transdiagnostic approach to investigating the relationship between sleep and working memory performance in children with neurological conditions. Transdiagnostic approaches, while typically not used when investigating neurological conditions, identify processes common to specific categories of psychiatric disorders (e.g., internalising disorders), and seek to produce one treatment protocol that is effective within that category of disorders (Harvey, 2008). In Study 2, not only was the presence of clinically-elevated levels of sleep problems established across several neurological diagnoses, but an association between sleep and working memory was also
demonstrated when data were analysed across the entire sample. These findings argue against a “disorder” focused approach, which considers stressors such as sleep problems as a by-product of the individual diagnosis that cannot be treated without first treating the diagnosed condition (Harvey, 2008). Rather, findings from Study 2 imply that sleep problems in children with neurological conditions may be a treatable risk factor that clinicians could address promptly and specifically, and that taking a transdiagnostic approach to sleep disturbance in these children may result in a service that is cost effective and easier to deliver. One promising intervention investigated by Stuttard, Beresford, Clarke, Beecham and Curtis (2015), is a relatively novel group intervention routinely delivered by a Child and Adolescent Mental Health Service Learning Disability team of nurses in England. The intervention is for parents of children with intellectual disabilities and/or autistic spectrum disorders and aims to teach parents specific strategies to manage sleep problem behaviours. At post-intervention (3- and 6-months), Stuttard et al. (2015) noted significant improvements in night-wakings, parent-set goals, and parents’ sense of efficacy. Moreover, the cost of the intervention was reportedly quite low. This exploratory study by Stuttard et al. (2015) not only provides support for the treatment of sleep disturbance as a transdiagnostic process in children with neurological conditions, but also underscores the potential for the development of a sleep group-intervention that can be implemented across a wide range of children’s neurological conditions.

Limitations

While the current research met the aims outlined at the beginning of the thesis, there were some unavoidable limitations. One potential limitation was the use of a subjective measure of sleep. The sleep questionnaire used in all three studies (Sleep Disturbance Scale for Children, Bruni et al., 1996) required parents to rate their child’s sleep behaviours retrospectively over the previous six months. Given the nature of the
participants included in the current research (e.g., children attending a
neuropsychological assessment or a school holiday program), we were unable to ask
parents in advance to monitor their child’s sleep patterns. The use of a sleep diary to
monitor participant’s sleep prior to their cognitive assessment would have allowed for a
more accurate parent-rating of their child’s sleep behaviour, particularly regarding the
measurement of sleep duration, sleep latency (time to fall asleep), and regularity of
sleep schedule. It should be noted that the sleep questionnaire used in the current
research was chosen specifically due to its sound psychometric properties, including
acceptable validity and reliability. Nonetheless, the subjective nature of the
questionnaire may have resulted in some children being incorrectly identified as having
(or not having) significant levels of sleep problems, daytime sleepiness, or snoring.
Further, we were unable to rule out possible over-reporting by parents of children from
clinical groups (e.g., neurological conditions). Studies have noted this as a possibility
when collecting subjective ratings of sleep from parents of children with clinical
diagnoses (e.g., Holley et al., 2014; Wiggs, Montgomery, & Stores, 2005). For example,
Holley et al. (2014) noted over-reporting of sleep problems by parents of children with
epilepsy due to anxiety surrounding their children’s sleep. While over-reporting in our
sample is a possibility, considerable variability between children with different
diagnoses in the Study 2 data suggests that there was no consistent bias in parental
report. Prevalence estimates of sleep problems in children with neurological conditions
have been reported to be as high as 75 to 80%, and typically range between 30 and 70%
(Dorris et al., 2008; Jan et al., 2008). Given the highest reported prevalence of sleep
problems in our clinical groups was approximately 48% (in the epilepsy group), and
transdiagnostically, the prevalence estimate was 34%, this again suggests that over-
reporting by parents was not a significant problem in the current research. It is
important to note that the sleep questionnaire was an effective tool that helped meet the
aims of the three studies. The use of parental report enabled the recruitment and collection of large (for sleep research) samples of data in short periods of time, which would not have been feasible if using actigraphy and polysomnography. Parental report was also advantageous when measuring sleep parameters in clinical populations of children. As mentioned previously, the use of polysomnography and actigraphy can be problematic when working with children with special needs (e.g., attention deficit hyperactivity disorder, intellectual disability, autism), as these children are often noncompliant with the setup of electrodes or continuously wearing an actigraph (Khatwa et al., 2013). Thus, while future studies will ideally include both objective and subjective measures of sleep (this will be discussed below), the use of parental report provided a cost and time effective form of sleep measurement which was appropriate to address the aims of the current research.

A second potential limitation to the current research was that performance on the spatial working memory measure in Study 2 was not comparable with performance on the nonverbal executive functioning measure in Study 3, due to differences in age and clinical background between the two samples in each study. As mentioned previously, spatial reasoning is a strong predictor of performance on the matrix reasoning task, thus, one might expect the impact of sleep to be similar on performance across spatial working memory and abstract reasoning tasks. Yet sleep was found to impact on abstract reasoning in children born very preterm, while no association was found between sleep and spatial working memory performance in children with neurological conditions. The use of two different populations of children meant that we were unable to rule out the possibility that the discrepancy may simply reflect confounding factors relating to characteristics specific to each study’s sample. For example, children born very preterm are at risk of a number factors that may affect brain development and subsequent cognitive functioning that children born to term (including children with
neurological conditions) are unlikely to be exposed to such as white matter injury (periventricular leukomalacia), inadequate provision of nutritional substrates and hormones essential to brain growth and development, medical complications (e.g., surgery, ventilation), and environmental stresses (separation from parents, invasive medical procedures) (Aylward, 2005; Peterson et al., 2000). It may be that children born very preterm are more vulnerable to the effects of poor sleep as a result of pre-existing cerebral injuries when compared to children with neurological conditions. Going forward, future studies may want to explore the relationship between sleep, spatial working memory performance, and performance on matrix reasoning tasks in one specific population of children.

A third limitation related to the use of the Matrix Reasoning subtest of the WISC-IV as a measure of executive functioning is that this measure is also commonly used as a measure of fluid intelligence. Interpreted in this way, some may argue that the findings from Study 3 indicate that children born preterm are impaired in terms of their fluid intelligence, and that sleep is impacting on this general ability in both groups. While the finding of poorer performance by children born preterm on tests of fluid intelligence has been shown before (e.g., Tideman, 2000), this may still result from difficulties with executive functioning impacting on their ability to complete these fluid intelligence tasks. Indeed, several authors have noted that executive functions are necessary when engaging in the problem solving/reasoning required in the Matrix Reasoning subtest of the WISC IV (e.g., Miller, 2007; Miller & Hale, 2008; Goldstein & Naglieri, 2013), and others have classified the Matrix Reasoning subtest as a task within the executive domain (e.g., Miller & Hale, 2008). Furthermore, many other studies have used the Matrix Reasoning subtest to assess executive functioning (e.g., McKinlay, Grace, Dalrymple-Alford, & Roger, 2009; Schiehser et al., 2011), and so, this subtest does appear to be generally accepted as a measure of executive functioning.
Given this, one plausible interpretation is that sleep does impact on executive functions, and that this, in turn, may impact performance on tests of fluid intelligence (regardless of birth type). While it is difficult to disentangle executive functions from fluid intelligence, future research would benefit from including a broader range of executive functioning tasks, as well as measures of fluid intelligence, to separate out the association between poor sleep and performance on these measures.

A final limitation relates to the sample size in the second study of Study 3. The number of children in each birth condition (very preterm, term) was relatively small compared to the first study in Study 3 and, consequently, the number of children within each birth condition with significant sleep problems was even smaller. Larger sample sizes in both birth conditions would have allowed for a better representation of the two populations of children and may have allowed for a clearer interpretation of the pattern of results. The trend towards an interaction between sleep problems and birth type, in addition to the finding of a significant impact of sleep problems on executive functioning in children born very preterm and not in children born to term, suggests there may have been a problem in power due to small sample sizes. As such, a sample size analysis was conducted using the software package, GPower (Faul & Erdfelder, 1992), with alpha of .05 and power set at .80. Based on the effects reported, 191 participants would be needed (100 more than in Study 3) in order for the effect size of .204 found in Study 3 to be statistically significant, were the study to be replicated. This would suggest that the failure to detect a significant interaction in Study 3 was not due to small sample sizes, but rather, is reflective of the small effect size. However, when the variability in executive functioning scores was examined for children with sleep problems in both the very preterm group and the term group, it was observed that there was a large amount of variability in the full term group which may have obscured any interaction. This would suggest that the recruitment of children specifically with sleep
problems in both preterm and term groups may have provided enough statistical power to detect a significant interaction.

**Future Directions**

In moving forward, the addition of objective sleep measures could be used to strengthen the conclusions reached in the current research and further extend our findings. For example, cardiorespiratory studies performed in the participant’s home could be used in combination with parental sleep logs to provide a more accurate estimate of the severity and frequency of snoring than parental report alone. These estimates could then be used to confirm whether the lack of an association between snoring and working memory was not simply a result of our snoring measure. Further, despite the challenges noted previously in the use of polysomnography, video-EEG (electroencephalogram)-polysomnography could be used to confirm whether the mechanism of sleep-related injury to prefrontal function was indeed sleep fragmentation, while simultaneously ruling out the presence of hypoxia and hypercarbia in our sample. The ability to record the different stages of sleep using EEG would mean that future studies could then record the sleep stage during which sleep fragmentation occurs and investigate whether disruption during specific sleep stages, or reduced time spent in specific sleep stages per sleep episode, is associated with working memory deficits and/or executive dysfunction. Interestingly, previous research has implicated stage two NREM sleep (N2), and more specifically, sleep spindles found predominantly in N2 sleep, as possibly underpinning intelligence and higher level cognition in children (Gruber et al., 2013). Indeed, higher levels of intelligence have been found to be associated with the amount of N2 sleep in school-aged children (Busby & Pivik, 1983) and reduced spindle frequency associated with better cognitive abilities (Urbain, Galer, Van Bogaert, & Peigneux, 2013). Importantly, studies have found reduced sleep spindle frequency to be associated with better performance on working memory tasks (e.g.,
Chatburn et al., 2013; Geiger et al., 2011; Gruber et al., 2013). For example, Gruber et al. (2013) investigated whether the specific characteristics of sleep spindles (e.g., duration, frequency, amplitude and density) were associated with performance on the perceptual reasoning, verbal comprehension, working memory, and processing speed subscales of the Wechsler Intelligence Scale for Children IV (WISC IV) in school-aged children. Results revealed that lower sleep spindle frequency was significantly associated with better performance on the working memory and perceptual reasoning subscales only. Aside from the few studies investigating sleep spindles and working memory performance in children, the association between working memory performance and sleep stages in children is an extremely under-researched area. The use of polysomnography in future studies investigating sleep and working memory performance in children may help to shed some light on the importance of each specific sleep stage.

When investigating sleep and cognition in typically developing children, future studies may also want to replicate a similar experimental study design to that of Vriend et al. (2013) and manipulate the duration of sleep. Vriend et al. (2012) originally employed a correlational study design to investigate sleep and cognition (including measures of working memory) in healthy, typically developing school-aged children. Consistent with Study 1, results from the Vriend et al. (2012) study revealed no association between sleep and the working memory measures. The researchers noted that a limitation to the study was the limited variability in sleep parameters, given that children identified as having “major” sleep problems were excluded from the study. While the criteria in Study 1 did not exclude children with sleep problems from participation, as mentioned previously, very few children were reported to have sleep problems in our sample, which is why Studies 2 and 3 recruited clinical populations of children known to have increased risk of sleep disturbance. However, rather than recruit
clinical populations of children, Vriend et al. (2013) introduced an experimental sleep manipulation to the same children from the earlier study (2012). Participants’ sleep duration was both increased and decreased by one hour, and performance was then compared across the two manipulation conditions. Results revealed an effect of reduced sleep on working memory performance, relative to the increased sleep condition. The Vriend et al. (2013) study design was strengthened by the fact that participants served as their own controls, which increased the sensitivity of the study design and helped to detect changes related to moderate sleep loss. Results from the Vriend et al. (2013) study highlight that sleep problems in typically developing children can impact upon working memory performance, but when conducting research investigating the relationship in this population of children, sleep restriction and/or extension may be the best approach to ensure variability in sleep parameters and to establish a causal effect.

Another direction for future research would be to include neuroimaging data, which was beyond the scope of the current research. As mentioned earlier, results from Study 2 suggest that neuroimaging (fMRI) in children with neurological conditions would be of benefit in helping to understand the discrepant findings in relation to the impact of poor sleep upon verbal and spatial working memory. Further, it would be interesting to compare patterns of brain activation during the matrix reasoning task and the spatial working memory task in both children with neurological conditions and children born very preterm. This would help to confirm whether differences in findings between the two studies were a result of the characteristics specific to each population of children, or whether children were incorporating verbal reasoning skills during performance on the matrix reasoning task. Future studies exploring sleep and working memory in clinical populations of children may also want to include the use of magnetic resonance imaging (MRI) to examine the relative size and volume of various brain areas and structures, in order to explore whether asymmetry in the left and right hemispheres
can explain the verbal and spatial discrepancy in Study 2. MRI can also provide information regarding pre-existing damage to specific brain areas, which may have influenced performance outcomes. Ideally, neuroimaging data would be collected longitudinally, given the developmental changes that occur in the brain. It may be that early insults at critical stages of development result in performance deficits that are not evident in children who received insults to similar brain regions at later stages of development (Ryan et al., 2015).

The current research also highlights the importance of future studies including measures of the subcomponents of working memory (e.g., storage capacity, processing speed, the central executive), in addition to including measures of both verbal and spatial working memory, when investigating the relationship between sleep and working memory in children. Only then can conclusions be drawn on the mechanisms that are impacted by poor sleep. While beyond the scope of this thesis, future studies may want to include multiple measures of verbal working memory, in addition to measures of general verbal abilities and language abilities, in order to investigate whether the effects of poor sleep are specific to verbal working memory or representative of more widespread difficulties with verbal or phonological processing problems or language difficulties. Similarly, when investigating the sleep-based neuropsychological perspective, it is recommended that future studies include measures of several executive functions, preferably tasks that isolate each executive function from other abilities. There are multiple executive functions thought to be associated with distinct frontal systems, which are distributed over a wide cerebral network including subcortical structures and thalamic pathways (Jurado & Rosselli, 2007). For example, monitoring behaviour has been found to activate the right dorsolateral prefrontal area, while the left dorsolateral prefrontal area is involved in phonemic verbal fluency, and both the right and left dorsolateral prefrontal areas, in addition to the superior medial
frontal lobe, are implicated in tasks that require cognitive switching (Frith et al., 1995; Stuss et al., 2002). Given that different executive functions are linked with different prefrontal areas, it is important to include a wide array of executive functions in future studies in order to clarify which executive processes are most at risk from sleep-related injury. In a similar vein, a strength of the current research was the inclusion of a measure of SES (maternal education). However, given the complexity of the SES construct, going forward, studies may want to include multiple measures of SES such as household income and wealth, perceived social status, and postcode.

One final future direction relates to the investigation of the vigilance hypothesis. While we included a measure of daytime sleepiness to test the vigilance hypothesis, future studies investigating sleep and cognition should, where possible, include measures of the alternative consequences of poor sleep (e.g., lapses in response thought to occur when micro-sleeps intrude into wakefulness following sleep deprivation). For example, the psychomotor vigilance task has been shown to be sensitive to sleep-related lapses in both children and adults (Goel, Rao, Durmer, & Dinges, 2009; Wilson, Dollman, Lushington, & Olds, 2010), with Wilson et al. (2010) demonstrating the successful application of a 5-minute psychomotor vigilance task with children. It may also be useful to include an objective measure of daytime sleepiness such as the Multiple Sleep Latency Test, which has been demonstrated as an effective tool in measuring daytime sleepiness in children (Aurora et al., 2012). The combination of a subjective and objective measure of daytime sleepiness will ensure an accurate interpretation of the relationship between daytime sleepiness and working memory performance in children.
Conclusions

Increasing evidence suggests that persistent sleep problems in children have a negative impact on their physical and neurocognitive development, mood and mood regulation, attention, behaviour, and general quality of life (Moore, Alison, & Rosen, 2006; Saunamaki & Jehkonen, 2007). This thesis makes an important, novel contribution to the literature examining sleep and cognitive functioning in children. Results revealed that decreased verbal working memory performance is associated with poor sleep quality in children born very preterm and in children with neurological conditions. This is worrying, given these children are already predisposed to cognitive difficulty given their medical histories.

This thesis revealed that sleep may be impacting upon an executive component of working memory, and that the effect of sleep upon children’s working memory was not simply due to them being sleepy after having slept poorly. Furthermore, this thesis calls for specificity within the sleep-based neuropsychological perspective. In particular, we propose that the mechanism by which sleep is impacting upon cognition is through sleep-related injury to specific neural substrates within prefrontal cortex mediating verbal (as opposed to spatial) executive functions. The high prevalence of poor sleep in children, coupled with the findings from the current research, drive home the importance of the early identification and treatment of sleep problems in school-aged children.

References


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