SLEEP & ATTENTION PROFILES IN CHILDREN WITH AUTISM SPECTRUM DISORDER

Submitted by

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A thesis submitted in fulfilment of the degree of

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School of Psychological Sciences

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Australia
To Aaron Koschel, for his love, support and patience
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ABSTRACT

Sleep serves a number of vital functions for the developing child and has been shown to have a number of critical implications for neurobehavioural functioning. A large number of school-age children do not get adequate sleep; the consequences of which can manifest in poorer behaviour and attention regulation outcomes; affecting subsequent learning and academic achievement. These associations are particularly concerning in school-age children with Autism Spectrum Disorder (ASD); with rates of sleep disturbance affecting up to 80%, and an often already compromised neurobehavioural and cognitive system.

The current thesis presents a series of papers which assess the profile of sleep and attentional difficulties, as well as interrelationships between the two, in school-age (6-12 years) children with and without ASD. Children’s naturally occurring sleep-wake profiles were obtained via 14-15 days of actigraphy monitoring and complimented by the parent-completed Children’s Sleep Habits Questionnaire (CSHQ) and measures of Attention-deficit hyperactivity disorder (ADHD) behaviour. Objective assessments of children’s’ cognitive attention functioning were obtained via the Attention Network Test for Children (ANT-C) and Wilding Attention Test for Children (WATT) immediately following two weeks of actigraphic monitoring.

Chapter 2 reviews existing literature around the nature of sleep and cognitive attentional functioning in children with ASD, as well as research exploring the impact children’s sleep duration and sleep quality has on their subsequent behaviour, attention and intellectual functioning. This review highlights the paucity of research studies which have examined the impact sleep difficulties may have on daytime cognitive attention and intellectual functioning in school-age children with ASD. Past ASD attentional and sleep research is additionally limited by heterogeneous ASD study groups and predominant reliance on subjective sleep measures to capture sleep.
Chapters 3 and 4 present cross-sectional comparisons of sleep and cognitive attention profiles in school-aged children with ASD and an age-matched subgroup of the TD cohort. The results of Paper 1 (Chapter 3) serve to reinforce difficulties in the initiation of sleep, as measured by actigraphy, as a core and persistent feature of the ASD sleep profile, as well as increased severity across all aspects of the parent-reported behavioural sleep profile. In addition to these core findings, actigraphic measurement revealed more between and within-child variability in sleep onset latency (SOL) in ASD compared to TD children, which has not been documented previously, and age-related differences in children’s sleep profiles. These findings not only emphasise the importance of exploring developmental differences when investigating sleep across the school-aged years but also demonstrate the unique contribution of including multi-modal sleep assessment measures to investigate sleep in children with ASD. Analysis of children’s cognitive attention development over middle childhood via the ANT-C and WATT (Chapter 4) revealed that children with ASD exhibit deficit functioning in aspects of both the orienting and alerting attention networks, and are less responsive to visual orienting cues in early childhood, compared to TD children. In addition, analysis of both tasks together suggest that switching and sustained attention subtests from the WATT are more sensitive to the attentional problems experienced by younger and older children with ASD. The findings of this paper not only serve to highlight the importance of considering developmental trajectories when examining attentional processes but also highlight the potential utility of the ANT-C and WATT as useful tools by with which to track overt and subtle deficits and improvements in attentional functioning in children with ASD.

Finally, Chapter 5 addresses gaps identified in the literature review by examination of associations between children’s objective sleep and objective/subjective attentional profiles. In both children with and without ASD, indicators of children’s sleep quality were found to
have associations with aspects of behavioural attention; however an association between increased difficulty with sustained attention and increased sleep fragmentation was evident in TD children only. Sleep duration did not appear to have any impact on behavioural or cognitive aspects of attention for either group. Together these findings suggest that sleep interventions which are targeted at improving the quality not quantity of sleep may have greater implications for subsequent daytime functioning.

Collectively, these findings address several key limitations of past research in order to more comprehensively characterise the profile of sleep and attentional problems affecting school-age children with ASD, and initiates exploration of the interrelationships between children’s naturally occurring sleep profiles and attentional functioning. The combined use of objective and subjective sleep measures served to further validate the increased frequency and severity of disturbed sleep in school-age children with ASD; suggesting that uniform screening for sleep disruption may be warranted in ASD, as well as the need for personalised, age-sensitive, and multimodal approaches to the management and treatment of sleep difficulties in this population. The early and pronounced deficits revealed in orienting attention in ASD indicate that abnormal functioning of this attention network may represent a primary disturbance of the disorder, and may, in fact, be associated with the emergence of ASD-related symptomology, and thus an appropriate target for early intervention. Together, findings support some relationship between the quality of children’s habitual sleep patterns and attentional functioning in children with and without ASD; however the increased severity and prevalence of sleep difficulties observed in ASD does not appear to be associated with increased difficulty on aspects of cognitive attention, suggesting that different brain networks may underlie difficulties in these areas.
LIST OF PRESENTATIONS DURING CANDIDATURE

Professional presentations


Awards and distinctions

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<td>ABBREVIATIONS</td>
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<tr>
<td>ADHD</td>
<td>Attention-Deficit Hyperactivity Disorder</td>
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<td>Autism Diagnostic Interview - Revised</td>
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<td>Aspergers Syndrome</td>
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<td>BR</td>
<td>Bedtime Resistance</td>
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<td>CSHQ</td>
<td>Children’s Sleep Habits Questionnaire</td>
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<td>DS</td>
<td>Daytime Sleepiness</td>
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<td>DSM</td>
<td>Diagnostic and Statistical Manual of Mental Disorders</td>
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<td>FSIQ</td>
<td>Full-Scale Intelligent Quotient</td>
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<tr>
<td>ID</td>
<td>Intellectual Disability</td>
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<td>NW</td>
<td>Night Wakings</td>
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<td>PDD-NOS</td>
<td>Pervasive Developmental Disorder Not Otherwise Specified</td>
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<td>PSG</td>
<td>Polysomnography</td>
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<td>SOD</td>
<td>Sleep Onset Delay</td>
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<td>Sleep Disordered Breathing</td>
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<td>Sleep Efficiency</td>
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<td>Social Responsiveness Scale</td>
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<td>Abbr</td>
<td>Full Form</td>
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<tr>
<td>SSRI</td>
<td>Selective Serotonin Reuptake Inhibitor</td>
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<td>TD</td>
<td>Typically Developing</td>
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<td>TIB</td>
<td>Time in Bed</td>
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<td>TST</td>
<td>Total Sleep Time</td>
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<tr>
<td>WASI</td>
<td>Wechsler Abbreviated Scale of Intelligence</td>
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<td>WASO</td>
<td>Wake After Sleep Onset</td>
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GENERAL DECLARATION
Monash University

Declaration for thesis based or partially based on conjointly published or unpublished work

In accordance with Monash University Doctorate Regulation 17.2 Doctor of Philosophy and Research Master’s regulations the following declarations are made:

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes three unpublished publications. The core theme of the thesis is sleep and attention in Autism Spectrum Disorder. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the candidate, working within the School of Psychological Sciences under the supervision of Professor Kim Cornish, Dr Russell Conduit, and Professor Nicole Rinehart.

The inclusion of co-authors reflects the fact that the work came from an active collaboration between researchers and acknowledges input into team-based research.
In the case of Chapters 3, 4, & 5 my contribution to the work involved the following:

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<td>Submitted</td>
<td>Study design, data collection, data analysis, interpretation of results, preparation of manuscript</td>
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<td>Submitted</td>
<td>Study design, data collection, data analysis, interpretation of results, preparation of manuscript</td>
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<td>Submitted</td>
<td>Study design, data collection, data analysis, interpretation of results, preparation of manuscript</td>
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I have renumbered sections of submitted papers in order to generate a consistent presentation within the thesis.

Student signature: [Redacted]  Date: 07/04/2016

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the student and co-authors’ contributions to this work.

Main Supervisor signature: [Redacted]  Date: 07/04/2016
ACKNOWLEDGEMENTS

The completion of this thesis has certainly been a challenging one, but one with which has also brought with it invaluable experiences, collaborations and friendships. There are several individuals, organisations, and funding bodies who have contributed to its successful completion and to whom I owe my sincerest gratitude.

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CHAPTER 1

INTRODUCTION

1.1. Research Overview

Sleep is a repetitive and active process which serves a number of vital functions for human physiological and neurocognitive health (Barone & Krieger, 2015; Krueger & Obal, 2003). Not surprisingly, sleep duration is at its highest during early childhood, when both the brain and body are undergoing their most rapid development, and declines gradually with age; with an average loss of approximately 6 minutes of sleep per night between the ages of 5 and 12 years (Galland, Taylor, Elder, & Herbison, 2012). The importance of sleep across childhood is reflected throughout the paediatric sleep literature, with inadequate sleep (both in terms of quantity and quality) linked to an array of poor physical and behavioural-cognitive outcomes including: emotional disturbance (Vriend et al., 2013), impairments in cognitive processing (Sadeh, Gruber, & Raviv, 2002; Vriend et al., 2013), behavioural problems (Aronen, Paavonen, Fjallberg, Soininen, & Torronen, 2000; Astill, Van der Heijden, Van Ijzendoorn, & Van Someren, 2012), reduced overall health (Smaldone, Honig, & Byrne, 2007; Snell, Adam, & Duncan, 2007), and an increased risk of injuries (Koulouglioti, Cole, & Kitzman, 2008). These links to children’s underlying physical and cognitive health are particularly concerning across the school-aged years (5-12 years), with research reporting rates of sleep disturbance affect up to 50% of neuro-typical school-aged children (Hodge, Carollo, Lewin, Hoffman, & Sweeney, 2014).

Autism Spectrum Disorder (ASD) is a complex and pervasive neurodevelopmental disorder characterised by impairments in social communication and social interaction, along
with restricted and repetitive behaviours, interests or activities (American Psychiatric Association, 2013). The relatively broad category of ASD encompasses those individuals’ with a previous and well–established DSM-IV-TR diagnosis of autism, Asperger disorder, and Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS; American Psychiatric Association, 2000), and is estimated to affect one in every 132 children worldwide (Baxter et al., 2015). ASDs are found to occur across all socioeconomic, ethnic and racial groups (American Psychiatric Association, 2000), but at a disproportionately higher rate in males than females; with a male/female ratio of 3:1 for autism, and a ratio of 4:1 for other ASDs (Baxter et al., 2015). ASD is characterised by considerable phenotypic heterogeneity (Kim, Lord, & Buxbaum, 2013). This includes notable variation in cognitive functioning with approximately 20-50% of individuals with ASD also affected by a comorbid diagnosis of intellectual disability (ID), while others score in the superior range on tests of intelligence (Charman et al., 2011). Considerable variability is also observed in terms of language functioning (non-verbal to fluent language skills), sensory and motor difficulties, adaptive functioning, and developmental course (Kim et al., 2013). Not surprisingly, such variation has significantly impacted, and in some cases impeded, research into the underlying aetiology, diagnosis, prognosis, and treatment of ASD (Georgiades et al., 2013), and highlighted the importance of conducting research in relatively well-defined populations of children with ASD.

Disturbances in sleep are one of the most consistently reported comorbid difficulties in children with ASD. It has been proposed that the high rate and diverse range of sleep problems affecting this population are underlined by a complex interaction between various biological, psychological, and environmental factors (Cortesi, Giannotti, Ivanenko, & Johnson, 2010; Richdale & Schreck, 2009). These include: 1) a neurobiological or genetic abnormality; with numerous studies demonstrating abnormal melatonin production in ASD
(Melke et al., 2008; Ritvo et al., 1993; Rossignol & Frye, 2011; Tordjman et al., 2012; Tordjman, Anderson, Pichard, Charbuy, & Touitou, 2005; Veatch et al., 2014); 2) frequently occurring psychological or behavioural co-morbidities proposed to exacerbate sleep difficulties (Allik, Larsson, & Smedje, 2006; DeVincent, Gadow, Delosh, & Geller, 2007; Goldman et al., 2011; Malow et al., 2006; Wiggs & Stores, 2004); and 3) social, environmental, and family factors, such as parenting style or poor bedtime routines, which are non-conducive to healthy sleep (Richdale & Schreck, 2009). Despite a large number of previous sleep studies in children with ASD several reoccurring limitations across the literature have limited knowledge in this area. These include a high reliance on subjective sleep measures which are poorly validated against objective sleep measures in ASD (Hodge, Parnell, Hoffman, & Sweeney, 2012), a heightened intolerance to the procedures involved in polysomnography (PSG) monitoring in a population in which sensory sensitivities are common, the use of broad and heterogeneous ASD samples which include children both with and without ID and span broad age-ranges, and in many cases, the absence of a TD control group with which comparisons can be made. As such, the precise nature of objectively-measured sleep difficulties affecting school-age children with ASD without comorbid ID remains unclear.

Converging evidence in TD children suggests that attention is an area of cognition on which sleep has a significant impact (Fallone, Acebo, Seifer, & Carskadon, 2005; Sadeh et al., 2002; Sadeh, Gruber, & Raviv, 2003; Touchette et al., 2007). This is particularly concerning in children with ASD; with inattention one of the most commonly reported behavioural concerns (Hartley, Sikora, & McCoy, 2008), and Attention-Deficit Hyperactivity Disorder (ADHD) the second most commonly occurring comorbid disorder (Simonoff et al., 2008). In addition, research utilising neuropsychological measures have also found deficit functioning in the underlying cognitive aspects of attention in children with ASD (Geurts,
Despite the highlighted links between sleep and attention, and alarming rates of both sleep problems and attention impairment in individuals with ASD, few studies to date have examined the relationship between these domains in children with ASD. In those that have, the primary focus has been on examining behavioural aspects of attention in the context of sleep quality; with poor sleep associated with increased ratings of both behavioural inattention and hyperactivity (Goldman, Malow, Newman, Roof, & Dykens, 2009; Goldman et al., 2011). In contrast, the extent to which sleep duration impacts behavioural attention, and sleep quality and sleep quantity affect cognitive attentional functioning in school-age children with ASD, remains to be determined.

This thesis builds on research to date by proposing a study of sleep and neurobehavioural functioning in primary school-aged children without ASD, in order to examine whether a relationship exists between these constructs, in this population. This research will examine differences in the sleep-wake profile in children aged 6 to 12 years with and without ASD without ID, using both actigraphy, and standardised parent-report sleep measures. Clinically, mapping the unique profile and trajectory of sleep in school-age children with ASD will help guide clinicians in the development and implementation of targeted sleep interventions for this age group. Scientifically, it also has potential implications for sleep assessment and analysis in this population. This thesis will also investigate whether school-age children with ASD without ID exhibit impairments in specific aspects of attentional functioning using computerised tasks designed specifically to engage children. Profiling subtle breakdowns in select components of attentional processing help further characterise the unique neuropsychological profile of children with ASD without ID; and may serve to help diagnostically differentiate children with ASD from other developmental disorder groups who also experience significant attentional problems, such as ADHD. Finally, to investigate the impact of sleep dysfunction on neurobehavioural function, this
thesis will also examine the extent to which sleep difficulties are associated with behavioural
difficulties and aspects of cognitive attention in both TD and ASD children. Collectively, this
research will contribute a substantial body of knowledge regarding the prevalence, severity,
and impact of sleep and attentional difficulties in children with ASD without ID.

1.2. Research Aims & Questions

The overarching aim of this research was to examine the objective sleep and attentional
profiles of school-age (6-12 years) children with a diagnosis of autism, Asperger’s syndrome,
or ASD, and, investigate whether any observed disturbances in sleep may be impacting
attentional functioning. This was achieved through a comprehensive sleep and
neurobehavioural test battery which included parent-reported measures of sleep (Children’s
Sleep Habits Questionnaire; sleep diary), ASD symptomology (Social Responsiveness Scale)
and behaviour (Strengths and Weaknesses of ADHD symptoms and Normal Behavior Scale;
The Conners Parent Rating Scale – 3rd Edition), two weeks of objective sleep measurement
via actigraphy, and objective tests of cognitive functioning (Wilding Abbreviated Intelligence
Scale) and attention (Attention Network Test for Children; Wilding Attention Test for
Children).

The primary research questions that are addressed by this thesis include:

1. Do school-age children with ASD without ID exhibit more actigraphy-measured sleep
disturbance than TD controls?
2. Do school-age children with ASD without ID exhibit different cognitive and
   behavioural attentional profiles than TD controls?
3. Are the Attention Network Test for Children (ANT-C), and the Wilding Attention Tests for Children (WATT), valid measures of cognitive attention in school-age children with and without ASD?

4. Does increased sleep disturbance have an impact on levels of cognitive (alerting, orienting and control) and behavioural attention in school-age children with and without ASD?

5. Does the relationship between sleep and attention differ between school-age children with ASD compared to their age-and-gender-matched TD peers?

1.3. Research Outline

This thesis is structured as a series of manuscripts that have been submitted to journals for publication. Additional sections of joining text have been included where appropriate to ensure that the thesis is both comprehensive and coherent. Chapter two reviews existing evidence for a relationship between sleep and neurobehavioural functioning in children and adolescents with ASD. The empirical papers examining the profile of sleep and attention in school-age children with ASD are contained within Chapters three and four, respectively. Chapter five is comprised of the final empirical paper, and explores whether a relationship exists between sleep and attentional functioning (both at a behaviour and cognitive level), and if so, whether this relationship differs between children with ASD and their age-and-gender-matched TD peers. Finally, Chapter six will evaluate the main research findings in view of the overarching aims of this thesis. Given that the thesis is presented in formatted journal style, there will be unavoidable repetition in some sections.
CHAPTER 2

EXAMINING SLEEP & ATTENTION PROFILES IN CHILDREN WITH AUTISM SPECTRUM DISORDER: THE IMPACT OF INADEQUATE SLEEP ON BEHAVIOUR, ATTENTION, & INTELLECTUAL FUNCTIONING

2.1. Introduction

In children without developmental disorders the evidence is mounting regarding the critical role sleep plays in daytime functioning; with research finding that inadequate sleep is linked to impairments in a number of cognitive domains including attention (Fallone, Acebo, Arnedt, Seifer, & Carskadon, 2001; Sadeh, Gruber, & Raviv, 2002; 2003) and executive functioning (Randazzo, Muehlbach, Schweitzer, & Walsh, 1998; Sadeh et al., 2002), is associated with the increased occurrence of problematic behaviours (Aronen, Paavonen, Fjallberg, Soininen, & Torronen, 2000; Astill, Van der Heijden, Van Ijzendoorn, & Van Someren, 2012; Touchette et al., 2007) and is related to increased academic difficulty and reduced school performance (Cooper, Kohler, & Blunden, 2012; Fallone, Acebo, Seifer, & Carskadon, 2005; Meijer, Habekote, & Van Den Wittenboer, 2000; Ravid, Afek, Suraiya, Shahar, & Pillar, 2009). These associations are particularly concerning in children with autism spectrum disorder (ASD) due to an often already compromised cognitive system, and disproportionately high rates of both sleep and attentional difficulties. In fact, sleep problems are one of the most commonly occurring concurrent clinical disorders (Xue, Brimacombe, Chaaban, Zimmerman-Bier, & Wagner, 2008), and attentional impairment is a core behavioural concern in children with ASD (Hartley, Sikora, & McCoy, 2008; Simonoff et al.,
The current paper reviews available data investigating the profile of both sleep and cognitive attention in children with ASD, as well as the relationship between sleep and behaviour, sleep and attention, and sleep and intellectual functioning in paediatric populations with ASD. In doing so, the authors seek to reveal which areas of cognition and behaviour are most vulnerable to disrupted sleep in children with ASD, and therefore require targeted intervention, as well as highlight areas requiring further investigation as they pertain to sleep and sleep disruption in ASD.

2.2. Autism Spectrum Disorder

Autism Spectrum Disorder is a neurodevelopmental disorder clinically defined by persistent impairments in reciprocal social and communicative interactions, and restricted and repetitive patterns of thought, behaviour or activities, such as the stereotyped use of objects (e.g. lining up one’s toys) or insistence on routine and sameness (American Psychiatric Association, 2013). Deficits in these two areas must be present during early development (although may not be fully expressed until later in development) and cause significant functional impairment. Whilst comorbid intellectual disability (ID) is common in ASD, with approximately 20-50% of individuals dually affected, cognitive functioning within the disorder is markedly varied; with some individuals with ASD performing within superior limits on traditional tests of intelligence (Charman et al., 2011). Up until the introduction of the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM), the diagnostic term ‘ASD’ was further subdivided into three groups of disorders: autism, Asperger syndrome (AS), and Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS; American Psychiatric Association, 2000). As such, those individuals with a previous and well-established DSM-IV-TR diagnosis of any of these three disorders are now encompassed under the single DSM-V diagnostic term, ASD, and are included in the current
review. Whilst the introduction of this new criterion for diagnosis was feared to reduce the ASD prevalence rate, recent estimates suggest 1 in every 132 children worldwide are affected with ASD (Baxter et al., 2015). ASD occurs across all socioeconomic, ethnic and racial groups (Developmental & Investigators, 2014) but affects males at a higher rate than females; with a male/female ratio of 3-4 to 1 (Baxter et al., 2015).

2.3. Attentional Functioning in ASD

Attention is complex multidimensional construct widely recognised as being fundamentally involved in many aspects of daily functioning. In defining attention it is useful to make the distinction between behavioural and cognitive components; where the former refers to overt behaviours such as distractibility and inattention, and the latter refers to the underlying cognitive aspects, such as the ability to identify and attend to what is relevant in one’s environment and ignore the irrelevant (Cornish & Wilding, 2010). Cognitive attention is posited to be made up of three separate, but interconnected brain networks coined the alerting or vigilance system, the orienting or selection system, and the executive control or conflict system (Posner & Petersen, 1990). The alerting network is described as involving the ability to attain and sustain a high state of alertness to incoming stimuli, in order to respond to it (Cornish & Wilding, 2010), and is most commonly referred to as “sustained attention” or “vigilance” in attention literature. The orienting network is described as the ability to overtly or covertly attend to selective sensory stimuli in our environment, and also to disengage attention from one’s current point of focus and move it to something else (Cornish & Wilding, 2010; Renner, Grofer Klinger, & Klinger, 2006). When discussing orienting attention it is important to differentiate between exogenous orienting, which is largely automatic and stimulus-driven, and endogenous attentional orienting, which is intentional and goal driven, as these different forms of orienting not only develop at different rates, but also
appears to require differing degrees of mental effort (Renner et al., 2006). Finally, executive control regulates attentional processes such as maintenance of conflicting information and inhibition (Posner & Petersen, 1990; Raz, 2004; Rothbart, Sheese, & Posner, 2007).

Whilst a large number of studies have examined attentional functioning in children with ASD, a clear understanding of the attentional profile in this population remains unclear. Additionally, while neuroimaging evidence suggests that Posner’s previously defined attentional networks are separate but interconnected, only one study to date has attempted to examine each attentional network simultaneously in the same cohort of children with ASD (Keehn, Lincoln, Muller, & Townsend, 2010). As such, each network will be considered separately in the current review in relation to its functioning in children with ASD.

2.3.1. Alerting Attention in ASD

The majority of studies examining the functioning of the alerting system in children with ASD have employed tasks which require participants to monitor a stream of incoming information, over a relatively long period of time, for the occurrence of a particular, and rarely occurring, target stimulus, and, for the most part report no deficits in performance in children with ASD both with and without comorbid ID. Early research by Garretson and colleagues reported children aged 4-19 years, diagnosed with autism disorder and ID, exhibit comparable performance to controls on a visual continuous performance test (CPT: Garretson, Fein, & Waterhouse, 1990). Children were required to identify a target line drawing within a stream of visual stimuli under four conditions; slow presentation with a tangible reward (pretzel or penny), fast presentation with a tangible reward (pretzel or penny), slow presentation with social reward (positive verbal reinforcement), and fast presentation with social reward (positive verbal reinforcement). Like controls, children with autism exhibited typical vigilance performance trends, with accuracy deteriorating over time,
and with task difficulty (slow versus fast conditions); with a decline in accuracy in all children found on the fast task. The only condition in which children with autism demonstrated significantly poorer performance than controls was with slow presentation with social reinforcement; suggesting that basic perceptual arousal is intact in children with autism, but that they may be driven by different motivational frameworks. More recent research has found similar results in individuals aged 7-21 years with autism without ID (Noterdaeme, Amorosa, Mildenberger, Sitter, & Minow, 2001), children aged 7-12 years with ASD without ID (May, Rinehart, Wilding, & Cornish, 2015), and children aged 6-14 with ASD whose level of intellectual functioning was not specified (Chan et al., 2009). In all three studies, similar performances were seen between control and ASD groups; with children with ASD performing similarly to TD children on simple reaction time tests tapping the alerting or arousal component of the alerting network across both auditory and visual computerised sustained attention tasks (Chan et al., 2009; Noterdaeme et al., 2001), and no group difference seen in number of errors made on a visual search vigilance task after verbal IQ was considered (May, Rinehart, et al., 2015). Interestingly, research comparing 21 children diagnosed with autism without ID, with 18 typically-developing (TD) children, and 23 children diagnosed with ADHD, on a visual ‘Sustained Attention to Response Task’ (SART), found that children with autism exhibited performances similar to controls whilst children with ADHD made a larger number of commission errors than both the control group and children with autism; suggesting impaired arousal processes may be a characteristic feature of ADHD but not ASD (Johnson et al., 2007). In addition to comparable performances on tests assessing sustained attention and vigilance, Keehn et al. (2010) reported intact attentional alerting in children and adolescents aged 8-19 years with ASD on a task designed specifically to test the efficiency of all three attentional networks: the Attention Network Test (ANT). Interestingly, whilst the ASD group did not differ from controls in
alerting network efficiency, unlike controls, their alerting efficiency scores were found to be significantly associated with efficiency in their executive control network; suggesting that equivalent alerting in children and adolescents with ASD may be due to compensatory executive processing (Keehn et al., 2010).

In contrast to the above studies, research conducted by Corbett & colleagues (Corbett & Constantine, 2006; Corbett, Constantine, Hendren, Rocke, & Ozonoff, 2009) and Murphy et al. (2014) report significant deficits in the alerting attention system in children, adolescents and adults with ASD. Utilising the ‘Integrated Visual and Auditory Continuous Performance test’, purported to rely equally on vigilance, speed, and focus, Corbett and colleagues reported poorer performance in children aged 7-12 years with ASD without ID compared to controls across both visual and auditory modalities; indicating poorer vigilance (Corbett & Constantine, 2006; Corbett et al., 2009). Murphy and colleagues found that adolescents and adults with ASD aged 11-35 years not only demonstrated slower reaction time and more intra-subject variability on a 12 minute sustained attention task, but also demonstrated reduced activation in brain regions associated with the alerting network (left and right inferior frontal cortical/superior temporal cortical, left middle frontal cortical, striato-thalamic, and right lateral cerebellar regions; Murphy et al., 2014). It is worth noting that unlike the majority of previous studies investigating alerting attention in ASD both Corbett and colleagues and Murphy et al. included subjects with ASD who also had ADHD symptomology. As such, it is possible that the observed deficits in the ASD group on this task, across both the visual and auditory modalities, were due to the overlapping co-morbid ADHD symptomology, rather than due to an inherent deficit related to ASD (Corbett et al., 2009). These findings, alongside the growing prevalence of co-morbid symptoms of ADHD in children with ASD, suggest that further investigation is needed regarding the functioning of this network in ASD, with utilisation of tasks such as the ANT, designed specifically to
assess each attentional network, alongside more traditional sustained attention/vigilance tasks likely to help elucidate the functioning of this attention network in ASD. In addition, it may be worth examining differences in performances on these tasks between children with ASD that do, and do not, have co-morbid ADHD symptomology.

2.3.2. Orienting Attention in ASD

Some of the earliest behavioural symptoms evident in children with ASD include failing to respond to one’s own name, abnormal gaze behaviour, and the absence of the use of gaze and gestures to engage others in interests. Some researchers have hypothesised that these deficits are linked to an underlying deficit in orienting attention to social stimuli (Dawson et al., 2004), while others have proposed that these early developing symptoms are not due to a specific deficit in the ability to orientate to social stimuli, but rather, that they may be indicative of a global impairment in the orienting attention network (Renner et al., 2006). A large number of studies have attempted to reveal the functioning of both exogenous (automatic, stimulus-driven) and endogenous (intentional, goal-driven) orienting in children with ASD in order to test this hypothesis. Most of these studies have utilised a computerised variant of Posner’s attentional cueing paradigm (1980); which utilises visual cues in order to manipulate attentional orienting. Such tasks require individuals to detect and respond to a target stimulus which can appear in a number of locations; although generally to the left or right of a central fixation point. In exogenous orienting tasks, abrupt-onset (150ms between cue and target) peripheral cues with 50% validity are typically used, while in endogenous orienting tasks, targets are proceeded by either a congruent (correctly orientates participant to upcoming target location) or incongruent (incorrectly orientates participant to upcoming target location) central directional cue, which are typically predictive (valid 80% of the time) in nature; although non-predictive cues (valid 50% of the time) can also be used (Pruett et al., 2011; Renner et al., 2006).
Research examining exogenous orienting largely supports the hypothesis that there is an underlying deficit in reflexive, automatic orienting in individuals with ASD. Townsend and colleagues have consistently found evidence for impaired orienting in adults with high-functioning ASD, with these individuals found to respond more slowly to target stimuli (Townsend et al., 2001), have more delayed early frontal electroencephalographic (EEG) scalp recorded responses; posited to reflect attention orienting (Townsend et al., 2001), and show reduced effects of cue validity (correctly versus incorrectly cued upcoming target location) when given only a short amount of time to shift attention (100ms delay between cue and target presentation; Townsend, Harris, & Courchesne, 1996). Similar findings have also been reported in children with ASD; with preschool and school-aged children with and without comorbid ID found to take significantly longer on average to orient and detect peripherally presented targets (Harris, Courchesne, Townsend, Carper, & Lord, 1999; Landry & Bryson, 2004), and children and adolescents with ASD without ID found to show smaller effects for the validity of peripheral cues than age-and-IQ-matched TD controls (e.g. 8% increase in accuracy in ASD group for correctly cued target location compared to 16% increase in accuracy in TD; Renner et al., 2006), and demonstrate reduced orienting scores compared to controls on the ANT; indicating impaired or slowed ability to shift attention in response to cues appearing in the location of upcoming targets (Keehn et al., 2010). Research conducted by Dawson and colleagues suggests that these deficits in exogenous orienting extend across other sensory modalities; with pre-school children with ASD also found to fail to orientate more frequently (by turning head and/or eyes) to both social and non-social auditory stimuli, than both TD children, and children with developmental delay without autism (Dawson et al., 2004). In contrast, research by Iarocci and Burack report no difference in performance between children with autism with ID with a mental age of 6-7 years, and mental-age matched TD controls on a computerised orienting flash cue task (Iarocci &
Burack, 2004). Due to a lack of further research looking at exogenous orienting in children with ASD who are more developmentally delayed, and differences in the methodologies between studies, it is unclear whether these discrepant findings are due to differences in participant populations, or because different tasks are in fact tapping different cognitive processes.

Unlike exogenous orienting studies, research investigating endogenous orienting is largely mixed. Whilst naturalistic observations and naturalistic studies interested in social orienting strongly support the notion that individuals with ASD have a deficit in their ability to utilise social cues in the environment to orient attention (Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998; Leekam, Hunnisett, & Moore, 1998; Leekam, Lopez, & Moore, 2000), these deficits are typically not represented in computer-based laboratory studies which manipulate social eye-gaze cues or non-social directional arrow cues to orientate participants to upcoming target stimuli. Most studies in fact report intact facilitation effects to social cues (faster responses to targets in cued versus uncued locations) in children and adults with ASD without ID, and no differences between ASD and control groups using dynamic emotional gaze cues (de Jong, van Engeland, & Kemner, 2008; Swettenham, Condie, Campbell, Milne, & Coleman, 2003; Uono, Sato, & Toichi, 2009), static schematic gaze cues (Pruett et al., 2011), and static gaze cues of photographed faces (Greene et al., 2011; Kylliainen & Hietanen, 2004; Vaidya et al., 2011). In contrast, two studies report no facilitation effect from valid versus invalid static schematic gaze cues in children and adults with ASD without ID (Goldberg et al., 2008; Ristic et al., 2005). Similarly, whilst several studies report comparable facilitation effects between children with ASD and controls in response to non-social arrow cues (Greene et al., 2011; Pruett et al., 2011; Vaidya et al., 2011), Wainwright-Sharp & Bryson report poorer orienting performance in children and adults with ASD when there is a short time between cue and stimulus onset (100ms; Wainwright-Sharp & Bryson,
Difficulties in endogenous orienting in ASD are also supported by studies utilising various set shifting tasks, with children and adults with autism found to make more preservation errors on the traditional version of the Wisconsin Card Sorting Task (WCST) and other human-administered variants, than age and IQ-matched typical controls (Griebling et al., 2010; Ozonoff & Jensen, 1999; Pellicano, 2007, 2010; Pellicano, Maybery, Durkin, & Maley, 2006; Prior & Hoffmann, 1990), and children aged 7-12 years with ASD without ID found to make significantly more errors on a computerised visual search switching task than their TD peers (May et al., 2015). Again, these findings have not been found consistently, with several studies utilising computer-based shifting tasks reporting unimpaired or mixed performance in ASD participants compared to controls; including the computerised WCST (Kaland, Smith, & Mortensen, 2008; Robinson, Goddard, Dritsche1, Wisley, & Howlin, 2009), the CANTAB Intradimensional/Extradimensional Shift Test (CANTAB-ID/ED; Corbett et al., 2009; Edgin & Pennington, 2005; Goldberg et al., 2005; Happe, Booth, Charlton, & Hughes, 2006; Landa & Goldberg, 2005; Sinzig, Morsch, Bruning, Schmidt, & Lehmkuhl, 2008), and other computerised variants (Dichter et al., 2010).

2.3.3. Executive Control in ASD

As previously mentioned the term ‘executive control’ refers to the overall regulation of attentional processes including maintenance of conflicting information and inhibition. The functioning of this network is often elucidated through the use of inhibition tasks such as the Stroop Test and Erikson’s Flanker Task, as both tasks require conflict monitoring and subsequent resolution. Similar to investigations of other attentional networks, research investigating the functioning of the executive control network in children with ASD are largely mixed (see Kenworthy, Yerys, Anthony, & Wallace, 2008 for a review). Investigators have posited that these discrepancies may exist due to the fact that there exist a number of
different aspects of inhibition and, that individuals with ASD experience specific deficits in some, but not all, aspects of inhibitory control (Christ, Kester, Bodner, & Miles, 2011; Hill, 2004). For example Hill (2004) hypothesised that prepotent response inhibition, typically measured using the Stroop task, is specifically impaired in ASD, while other aspects of inhibition, such as resistance to distracter interference, are intact. Contrary to this hypothesis, although several studies have found impaired ability to withhold a prepotent response in children and adults with ASD, on four different tasks (the computerised version of the Stroop being one: Corbett et al., 2009; Mosconi et al., 2009; Robinson et al., 2009), comparable performances between ASD and control groups on traditional, human-administered, and computerised versions of the Stroop are also reported (Adams & Jarrold, 2009; Christ, Holt, White, & Green, 2007; Christ et al., 2011; Goldberg et al., 2005; Happe et al., 2006; Hill & Bird, 2006; Lopez, Lincoln, Ozonoff, & Lai, 2005). Studies assessing resistance to distracter interference using a computerised flanker paradigm are also conflicting. Whilst Christ and colleagues report impaired performance on a computerised interference test using shape/symbol and fish stimuli in children aged 6-12 years (mean age: 8.2 years; Christ et al., 2007) and 8-18 years (mean age: 13.1 years) with ASD (Christ et al., 2011), Keehn et al. report no differences between children aged 8-19 years (mean age: 13.9 years) with ASD without ID and controls on an arrow stimuli version of the task (Keehn et al., 2010). It is possible that these inconsistencies are due to underlying differences between ASD cohorts, with the absence of comorbid ID not outlined by Christ and colleagues, and different age ranges included in all three studies. Consideration of the potential impact of age on task performance is highlighted by Christ et al. (2011) who found that impairment in resistance to distracter interference was more apparent in younger versus older individuals with ASD, and should be considered in future studies.
2.3.4. Attentional functioning in ASD – A Summary of Findings

Taken together these findings suggest that children with ASD exhibit impairments in exogenous orienting, but that the functioning of the alerting network may depend on the absence or presence of comorbid ADHD; with impairment in this network reported in children with ASD who also demonstrated elevated levels of ADHD symptomology. Disparate findings in terms of endogenous orienting and executive control, however are hard to reconcile. This is due to the large diversity of attention measures employed between, and within, studies and differences between ASD cohorts. One task which may help more clearly elucidate the functioning of all three of these attention networks in children with ASD is the Attention Network Test (ANT) developed by Fan and colleagues (Fan, McCandliss, Sommer, Raz, & Posner, 2002). This experimental RT task is built upon many neuroimaging studies, provides a measure of all three attention networks simultaneously, and has subsequently been adapted and developed into a child-friendly version, the Attention Network test for Children (ANT-C), in order to better study the development of these networks in childhood (Rueda et al., 2004). Despite successful use of both the ANT, and ANT-C, to measure the cognitive profile of attention in other clinical cohorts, to date, only one known study has attempted to examine each attentional network in the same cohort of children with ASD (Keehn et al., 2010); and none have done so using the child-friendly version.

2.4. Sleep problems in children with ASD

As previously highlighted, sleep disturbances occur at a disproportionately high rate in children with ASD; with parent-reported prevalence rates ranging between 66-81% in children with ASD compared to 26-50% in TD children (Couturier et al., 2005; Hodge, Carollo, Lewin, Hoffman, & Sweeney, 2014; Souders et al., 2009). This high prevalence not only persists across age groups; with high rates of sleep problems reported in toddlers
primary school-aged children (Goldman et al., 2012; Mayes & Calhoun, 2009), and adolescents and adults with ASD (Goldman et al., 2012; Limoges, Mottron, Bolduc, Berthiaume, & Godbout, 2005; Mayes & Calhoun, 2009), but are also found to be common across cognitive level (Johnson, Turner, Foldes, Malow, & Wiggs, 2012; Mayes & Calhoun, 2009), ethnicity, and socio-economic background (Mayes & Calhoun, 2009). In addition, children who manifest problems typical of ASD (classified as having autism spectrum problems), but without a diagnosis of ASD, have been found to develop more parent-reported sleep problems over time, and exhibit lower rates of remission of these sleep problems, than controls without any ASD symptomology (Sivertsen, Posserud, Gillberg, Lundervold, & Hysing, 2012).

2.4.1. Types of Sleep Problems Experienced in ASD

The majority of previous research studies examining the profile of sleep in children and adolescents with ASD have utilised parental reports. The most common parent-reported sleep concerns are reduced sleep duration due to sleep onset problems (Couturier et al., 2005; Williams, Sears, & Allard, 2004; Goldman et al., 2012; Mayes & Calhoun, 2009; Paavonen et al., 2008; Souders et al., 2009; Tsai et al., 2012), and poor sleep maintenance; with frequent night awakenings (Williams et al., 2004; Goldman et al., 2012; Mayes & Calhoun, 2009; Paavonen et al., 2008; Souders et al., 2009). Parasomnias and increased sleep anxiety (Couturier et al., 2005; Goldman et al., 2012; Paavonen et al., 2008; Schreck & Mulick, 2000; Souders et al., 2009), as well as sleep-related breathing and movement disorders (Williams et al., 2004; Liu, Hubbard, Fabes, & Adam, 2006; Schreck & Mulick, 2000), are also reported to occur more frequently. Research utilising objective sleep measurement such as actigraphy and polysomnography (PSG) largely confirm these parental reports, with children and adults
with ASD found to have poorer sleep efficiency, (Goldman et al., 2009; Limoges et al., 2005; Maski et al., 2015), reduced sleep overall (Elia et al., 2000), increased sleep onset latency (Allik, Larsson, & Smedje, 2006; Goldman et al., 2009; Limoges et al., 2005; Maski et al., 2015; Souders et al., 2009), and more frequent sleep awakenings; which are longer in duration (Goldman et al., 2009; Limoges et al., 2005; Maski et al., 2015; Souders et al., 2009), than their TD peers. In addition, whilst high rates of sleep problems are reported across all age groups in ASD, research examining parent-reported sleep problems in children aged 3-18 years with a diagnosis of ASD (autism, Asperger’s syndrome, or Pervasive Developmental Disorder-Not Otherwise specified) found that different age groups experience differ types of sleep problems (Goldman et al., 2012). Specifically, children aged 5 years and younger are reported to experience more parasomnias, bedtime resistance, and night waking compared to children aged 7 years and older, sleep behaviours are similar between children aged 5 to 7 years and children aged 7 to 11 years, whilst older children and adolescents experience more problems with delayed sleep onset, shorter overall sleep duration, and increased daytime sleepiness. Given the wide-ranging nature of these sleep difficulties, and reported age-related differences, it is important that future research studies seek to disentangle which aspects of the ASD sleep profile, within specific age cohorts, are in fact impacting neurobehavioural functioning in order for targeted and effective interventions to be applied.

2.4.2. Disrupted Sleep Architecture in ASD

Sleep architecture refers to the underlying structure and organisation of sleep; including the cyclical shift between non-rapid eye movement (NREM) and rapid eye-movement (REM) sleep stages (Altevogt & Colten, 2006). PSG studies have demonstrated a number of abnormalities in REM sleep; with children, adolescents, and young adults with autism and
intellectual disability (ID) demonstrating reduced REM sleep latency (Miano et al., 2007), and individuals with ASD both with and without ID found to spend a reduced percentage of time in REM sleep overall than TD controls (Diomedi et al., 1999; Maski et al., 2015). In addition, children and adults with Asperger’s syndrome have been found to shift into REM sleep from waking more often than TD controls (Godbout, Bergeron, Limoges, Stip, & Mottron, 2000), and adults with ASD without ID or any sleep complaints have been found to have a reduced number of rapid eye movements per hour during REM sleep (Limoges et al., 2005). Abnormalities are also present in NREM sleep. In children, differences have been noted in cyclic alternating pattern (CAP) rates; which refers to a period of distinct electroencephalogram (EEG) activity (e.g. k-complexes and sleep spindles of higher or lower voltage), that occur against a background of EEG activity during NREM sleep, and are followed by an episode of more stable sleep (Bruni et al., 2010). In comparison to TD children, children with autism and ID aged 3-19 years have been found to have a lower CAP rate during slow wave sleep (SWS; Miano et al., 2007), whilst children with Asperger’s syndrome aged 7-15 years have been found to have a reduced CAP rate during the first two stages of NREM sleep (Bruni et al., 2007). In addition, differences in sleep architecture have been noted between children with autism without ID and children with Asperger’s syndrome, with the latter found to have a higher CAP rate during SWS, but a decreased CAP rate in Stage 2 of NREM sleep (Bruni et al., 2007). These differences in SWS CAP rates further implicate frontal lobe dysfunction in ASD; with frontal lobe regions known to play a key role in the generation of these slow waves (Ferri, Bruni, Miano, & Terzano, 2005).

2.5. The relationship between sleep, behaviour, and attentional functioning

The underlying brain mechanisms by which sleep disturbance may contribute to deficits in neurobehavioural functioning are not known, although several hypotheses have been
proposed. Research in adult populations have implicated the prefrontal cortex, with this brain area implicated as an important interface for regulation of higher cognitive functions, sleep, and emotional functioning (Dahl, 1996; Miano et al., 2007), and research finding that one night of complete sleep deprivation is associated with markedly reduced prefrontal activation, and decreased performance on an assessment of arithmetic ability (Drummond et al., 1999). Other research suggests changes in neural circuitry occurs following sleep disruption, and that these changes underline the disturbances subsequently seen in behaviour; with research reporting reduced communication between the prefrontal cortex and amygdala in adults following sleep deprivation (Van Der Helm, Gujar, & Walker, 2010), and reduced activation in the caudate nucleus of children aged 11-13 years with reduced sleep time and sleep quality during a reward anticipation and reward outcome task (Holm et al., 2009). Disturbances in this underlying sleep architecture have also been proposed to drive impairments in neurobehavioural functioning, with research demonstrating associations between sleep spindle activity and several neurobehavioural domains including internalising and externalising behaviours, learning, reading ability, and social behaviour (Bruni et al., 2009; Mikoteit et al., 2013), and slow wave sleep (SWS) hypothesised to impact cognition, particularly executive functioning, via fronto-cortical brain regions (Ringli & Huber, 2011).

2.5.1. *Sleep is linked to behavioural problems in ASD*

In TD children, sleep disruption is linked to the increased occurrence of behavioural problems (Astill et al., 2012; Maski & Kothare, 2013). This association is particularly concerning in children with ASD, in which co-occurring behavioural disorders such as ADHD and oppositional defiant disorder are relatively common (Simonoff et al., 2008), and rates of sleep disturbances are high (Richdale & Schreck, 2009). Research examining the relationship between sleep and behaviour in ASD child and adolescent populations is
summarised in Table 1. Together, studies investigating the relationship between sleep and autism symptomology suggest that a significant and bi-directional relationship may exist between these constructs in children with ASD. Specifically, research has not only found that increased sleep disturbance is significantly associated with greater social (May, Cornish, Conduit, Rajaratnam, & Rinehart, 2015; Nadeau et al., 2015; Schreck, Mulick, & Smith, 2004; Taylor, Schreck, & Mulick, 2012), communication (Hoffman et al., 2005; Park et al., 2012; Tudor, Hoffman, & Sweeney, 2012), and repetitive and stereotyped behaviour deficits (Goldman et al., 2009; 2011; Hoffman et al., 2005; Park et al., 2012; Schreck et al., 2004; Tudor et al., 2012), but also that greater severity of autism symptoms predicts more sleep disturbance (Hollway, Aman, & Butter, 2013; Mayes & Calhoun, 2009) in children with ASD. In addition, research has also shown that, similarly to TD children, sleep problems are also associated with: the increased occurrence of a number of problematic externalising and internalising behaviours including aggression, impulsivity, inattention, hyperactivity (Allik et al., 2006; DeVincent, Gadow, Delosh, & Geller, 2007; Goldman et al., 2009; 2011; Henderson, Barry, Bader, & Jordan, 2011; Hill et al., 2014; Liu et al., 2006; May, Cornish, et al., 2015; Mayes & Calhoun, 2009; Mazurek, Kanne, & Wodka, 2013; Nadeau et al., 2015; Sikora, Johnson, Clemons, & Katz, 2012), higher ratings of oppositional and total behaviour problems (Adams, Matson, & Jang, 2014; Anders, Iosif, Schwichtenberg, Tang, & Goodlin-Jones, 2012; DeVincent et al., 2007; Fadini et al., 2015; Rzepecka, McKenzie, McClure, & Murphy, 2011), and poorer adaptive functioning (Sikora et al., 2012; Taylor et al., 2012), in preschool, school-age, and adolescents with ASD. Whilst these studies are useful in highlighting the wide-spread effects sleep disruption may be having on behavioural functioning, the inclusion of children with ASD across broad age ranges and cognitive levels (ID versus no ID) make it difficult to disentangle whether associations between sleep and behaviour may differ between different age groups and the relative impact of IQ on these
relationships. In addition, few studies to date have explored the relationship between objectively-measured sleep and behavioural functioning in children with ASD, with most relying solely on parent-reported subjective sleep measures.
Table 1. Research exploring the relationship between sleep and behaviour in preschool, school-age, and adolescent children with ASD

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Age groups</th>
<th>Age range</th>
<th>Sample</th>
<th>Sleep &amp; behaviour measures</th>
<th>Core findings regarding sleep &amp; behaviour</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Nadeau et al., 2015)</td>
<td>Cross-sectional</td>
<td>School-age - Adolescence</td>
<td>7-16 years</td>
<td>102 individuals with ASD &amp; comorbid anxiety</td>
<td>PARS, MASC-P, SRS, CBCL</td>
<td>Sleep-related problems were associated with ratings of social deficits, &amp; internalising &amp; externalising symptoms</td>
</tr>
<tr>
<td>(Fadini et al., 2015)</td>
<td>Cross-sectional</td>
<td>Preschool - Adolescence</td>
<td>4-18 years</td>
<td>45 children with ASD, 56 TD children</td>
<td>SDSC, CBCL</td>
<td>Higher ‘disorders of excessive somnolence’ scores were associated with more total behaviour problems in ASD.</td>
</tr>
<tr>
<td>(May et al., 2015)</td>
<td>Longitudinal</td>
<td>School-Age</td>
<td>7-12 years</td>
<td>46 children with ASD, 38 TD children</td>
<td>CSHQ, SRS; Conners-3</td>
<td>Decreased sleep disturbance over 1 year was associated with improved social ability in ASD. Sleep disturbance at Time 1 &amp; 2 were associated with social difficulties, aggression, &amp; hyperactivity. Sleep disturbance did not predict later aggression, autism symptoms or hyperactivity.</td>
</tr>
<tr>
<td>(Hill et al., 2014)</td>
<td>Cross-sectional</td>
<td>Preschool- Adolescence</td>
<td>2-16 years</td>
<td>400 individuals with ASD</td>
<td>CSHQ, CBCL</td>
<td>Aggressive behaviour problems were associated with more sleep difficulties</td>
</tr>
<tr>
<td>(Adams et al., 2014)</td>
<td>Cross-sectional</td>
<td>Preschool - Adolescence</td>
<td>2-18 years</td>
<td>311 individuals with ASD</td>
<td>ASD-C</td>
<td>Children with severe sleep problems had higher ratings of total challenging behaviours than children with mild or no sleep problems</td>
</tr>
<tr>
<td>(Richdale, et al., 2014)</td>
<td>Cross-sectional</td>
<td>Adolescence</td>
<td>15-17 years</td>
<td>27 adolescents with ASD, 27 TD adolescents</td>
<td>SD, ACT, mSHS, CSRQ,</td>
<td>In ASD parent-reported &amp; objectively-measured sleep variables were associated with daytime functioning scores. Sleep variables accounted for 57% of variance in daytime functioning symptoms of insufficient sleep in ASD.</td>
</tr>
<tr>
<td>(Mazurek et al., 2013)</td>
<td>Cross-sectional</td>
<td>Preschool - Adolescence</td>
<td>2-17 years</td>
<td>1584 individuals with ASD</td>
<td>ATS-P, CSHQ</td>
<td>Sleep problems were strongly associated with aggression</td>
</tr>
<tr>
<td>(Hollway et al., 2013)</td>
<td>Cross-sectional</td>
<td>Preschool - Adolescence</td>
<td>2-17 years</td>
<td>1583 individuals with ASD</td>
<td>CSHQ, ADOS, SSP</td>
<td>Severity of autism symptoms predicted overall sleep disturbance &amp; bedtime resistance. Sensory sensitivities predicted overall sleep disturbance &amp; sleep anxiety.</td>
</tr>
<tr>
<td>(Anders et al., 2012)</td>
<td>Longitudinal</td>
<td>Preschool</td>
<td>2-5 years</td>
<td>68 children with ASD,</td>
<td>ACT, CSHQ, CBCL, MSEL,</td>
<td>Parent-reported sleep disturbance, but not actigraphic sleep, was associated with more daytime sleepiness &amp; behaviour problems in</td>
</tr>
<tr>
<td>Study References</td>
<td>Study Design</td>
<td>Age Range</td>
<td>Participants</td>
<td>Measures</td>
<td>Findings</td>
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<tr>
<td>(Park et al., 2012)</td>
<td>Cross-sectional</td>
<td>4-15 years</td>
<td>166 children with ASD, 111 ASD siblings</td>
<td>CSHQ, ADI-R</td>
<td>Communication problems &amp; repetitive stereotyped behaviours were associated with increased risk of sleep problems in ASD.</td>
<td></td>
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<tr>
<td>(Sikora et al., 2012)</td>
<td>Cross-sectional</td>
<td>4-10 years</td>
<td>1193 children with ASD</td>
<td>CSHQ, CBCL, MSEL, VABS</td>
<td>Children with sleep problems had more externalising/externalising problems, &amp; poorer adaptive skills than those without sleep problems.</td>
<td></td>
</tr>
<tr>
<td>(Taylor et al., 2012)</td>
<td>Cross-sectional</td>
<td>1-10 years</td>
<td>335 children with ASD</td>
<td>BEDS, VABS, SIB-R</td>
<td>Children who slept fewer hours per night had lower adaptive functioning, daily living skills &amp; poorer socialisation &amp; motor development.</td>
<td></td>
</tr>
<tr>
<td>(Tudor et al., 2012)</td>
<td>Cross-sectional</td>
<td>3-18 years</td>
<td>109 individuals with ASD</td>
<td>CSHQ, GARS</td>
<td>Sleep onset delay &amp; sleep duration were positively associated with autism symptoms &amp; autism severity. Sleep onset delay was the strongest predictor of communication deficit, stereotyped behaviour, &amp; autism severity.</td>
<td></td>
</tr>
<tr>
<td>(Goldman et al., 2011)</td>
<td>Cross-sectional</td>
<td>2-18 years</td>
<td>1784 individuals with ASD</td>
<td>CSHQ, PCQ</td>
<td>Children reported to be poor sleepers also had more problems with aggression, hyperactivity, stereotypy &amp; repetitive &amp; restrictive behaviours than good sleepers</td>
<td></td>
</tr>
<tr>
<td>(Henderson et al., 2011)</td>
<td>Cross-sectional</td>
<td>6-12 years</td>
<td>58 children with ASD, 57 children without ASD</td>
<td>BRQ, CSHS, CSWS, CBCL</td>
<td>Poor sleep quality and sleep hygiene were associated with higher levels of externalising behaviour in ASD.</td>
<td></td>
</tr>
<tr>
<td>(Rzepecka et al., 2011)</td>
<td>Cross-sectional</td>
<td>5-18 years</td>
<td>187 children with an ID and/or ASD</td>
<td>CSHQ, ABC-C</td>
<td>Higher levels of sleep problems were associated with higher levels of challenging behaviour in children with ID and/or ASD. Sleep problems were the strongest predictor of challenging behaviour scores in this population.</td>
<td></td>
</tr>
<tr>
<td>(Goldman et al., 2009)</td>
<td>Cross-sectional</td>
<td>4-10 years</td>
<td>42 children with ASD, 16 TD children</td>
<td>PSG, ACT, CSHQ, PCQ, RBS-R, CBCL</td>
<td>Parent-defined poor sleepers in the ASD group also had higher ratings of inattention, hyperactivity, &amp; compulsive &amp; ritualistic traits. In children with ASD, ACT WASO was associated with hyperactivity, and sleep fragmentation was associated with repetitive &amp; restrictive behaviours.</td>
<td></td>
</tr>
<tr>
<td>(Goodlin-Jones,</td>
<td>Cross-sectional</td>
<td>2-5 years</td>
<td>66 children with ASD, ACT, CBCL,</td>
<td></td>
<td>ADHD profiles were associated with parent-reported sleep</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Age range</td>
<td>Sample size</td>
<td>Measures</td>
<td>Findings</td>
<td></td>
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<tr>
<td>(Goodlin-Jones, Tang et al. 2009)</td>
<td>Cross-sectional</td>
<td>Preschool 2-5 years</td>
<td>68 children with ASD, 57 children with DD, 69 TD children</td>
<td>ACT, CBCL, ESS, MSEL</td>
<td>Parent-reported, but not ACT-measured, sleep problems, were associated with poorer daytime behaviour after controlling for age and diagnosis.</td>
<td></td>
</tr>
<tr>
<td>(DeVincent et al., 2007)</td>
<td>Cross-sectional</td>
<td>Preschool 3-5 years</td>
<td>112 children with PDD, 497 TD children</td>
<td>Early Childhood Inventory-4,</td>
<td>Children with sleep problems also had more symptoms of ADHD and oppositional defiant disorder than good sleepers across groups.</td>
<td></td>
</tr>
<tr>
<td>(Liu et al., 2006)</td>
<td>Cross-sectional</td>
<td>Preschool - Adolescence 2-18 years</td>
<td>167 children with ASD</td>
<td>CSHQ, PSQ</td>
<td>Both hypersensitivity &amp; ADHD symptomology, along with younger age, co-sleeping, epilepsy, asthma, bedtime routine, medication, and a family history of sleep problems, were associated with parent-reported sleep problems.</td>
<td></td>
</tr>
<tr>
<td>(Allik et al., 2006)</td>
<td>Cross-sectional</td>
<td>School-age 8-12 years</td>
<td>32 children with ASD, 32 TD children</td>
<td>ACT, Pediatric sleep-wake behaviour scale, ASSQ, SDQ</td>
<td>Children classified as having insomnia based parent-report also had more autism symptomology and more emotional and hyperactivity symptoms than those without insomnia.</td>
<td></td>
</tr>
<tr>
<td>(Hoffman et al., 2005)</td>
<td>Cross-sectional</td>
<td>Preschool - Adolescence 4-15 years</td>
<td>80 individuals with ASD</td>
<td>CSHQ, GARS</td>
<td>Sleep problems were associated with autism diagnostic domains. SDB predicted increased problems with stereotyped behaviour &amp; social interactions, as well as overall level of autism. Parasomnias &amp; sleep duration predicted children’s level of developmental disturbance.</td>
<td></td>
</tr>
<tr>
<td>(Schreck et al., 2004)</td>
<td>Cross-sectional</td>
<td>School-age 5-12 years</td>
<td>55 children with ASD</td>
<td>BEDS, PSQ, GARS</td>
<td>Fewer hours of sleep per night predicted severity of autism symptoms, social skill deficits, &amp; stereotypic behaviour.</td>
<td></td>
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</table>

*ABC-C Abhorrent Behaviour Checklist-Community; ACT Actigraphy; ADI-R, ADOS, ASD Autism Spectrum Disorder; ASD-C Autism Spectrum Disorder – child version; ASSQ, ATS-P Autism Parent Network – Parent Survey; BEDS, BRQ Bedtime Routines Questionnaire; CBCL Child Behavior Checklist; Conners-3, CSHS Children’s Sleep*
Hygiene Scale; CSHQ Children’s Sleep Habits Questionnaire; CSRQ Chronic Sleep Reduction Questionnaire; CSWS Children’s Sleep-Wake Scale; ESS Epworth Sleepiness Scale; GARS Gilliam Autism Rating Scale; MASC-P Multidimensional Anxiety Scale for Children-Parent; MSEL, mSHS Modified Sleep Habits Survey; PARS Pediatric Anxiety Rating Scale; PBS, PCQ Parental Concerns Questionnaire; PSG, PSQ, RBS-R Repetitive Behavior Scale – Revised; SD, SDSC Sleep Disturbance Scale for Children; SDQ, SIB-R Scales of independent behaviour-revised; SRS Social Responsiveness Scale; SSP, TD Typically-developing; WISC, VABS Vineland Adaptive Behavior Scales.
2.5.2. Inadequate sleep impacts cognitive attention and intellectual functioning in ASD

Although sleep disruption and reduced sleep quantity are known to affect cognition and academic achievement in TD children (Buckhalt, El-Sheikh, & Keller, 2007; Fallone et al., 2005; Sadeh et al., 2003; Steenari et al., 2003), the relationship between sleep and cognitive functioning in children with ASD remains underexplored. The following section reviews the few studies which have explored the relationship between sleep quantity, sleep quality or sleep architecture in association with performance on objective tests of attention and intelligence, in children and/or adolescents with ASD.

In TD children inadequate sleep (reduced duration and/or reduced sleep quality) has been linked to reduced performance on tests of sustained attention (Fallone et al., 2001; Sadeh, Gruber, & Raviv, 2002) and response inhibition (Fallone et al., 2001), and extended sleep for several nights has been found to be associated with improved performance on tests of attentional capacity (Sadeh et al., 2003). Research conducted in adolescents and young adults aged 16-27 years with ASD without ID has found that, contrary to research in TD children, PSG indicators of poor sleep (sleep onset latency, percentage of time spent in stage 1 sleep, and percentage of time spent awake after sleep onset) showed no association with performance on a task of sustained attention, but did show significant associations with selective attention: with positive correlations observed between sleep onset latency and reaction time, sleep onset time and number of errors made, and percentage of time spent in stage 1 sleep and number of errors made (Limoges, Bolduc, Berthiaume, Mottron, & Godbout, 2013). In addition, one paediatric study has shown that reduced parent-reported sleep duration is associated with more preservation errors on the Wisconsin Card Sort Task (WCST) in children aged 7-14 years with ASD; indicating reduced cognitive flexibility/attentional switching (Memari et al., 2013). Whilst poor sleep has been associated with worse performance on tests of working memory (WM) in TD children (Steenari et al.,
2003), Mayes & Calhoun (2009) found no association between parent-reported sleep disturbance scores and overall working memory ability in school-age children with ASD of mixed cognitive levels (included children both with and without comorbid ID).

Attention is considered a source, determinant, and constitute of intelligence (Schweizer, 2010). In fact Schweizer et al. have demonstrated substantial links between a large variety of attention subtypes and intelligence, and a large overlap between different subtypes of attention in predicting intelligence (Schweizer, Moosbrugger, & Goldhammer, 2005). Given these links, and research in TD populations which has shown that reduced sleep and specific sleep problems have a negative impact on performance on cognition ability measures (Curcio, Ferrara, & De Gennaro, 2006; Gruber et al., 2010; Touchette et al., 2007), research investigating the relationship between sleep and general intellectual in ASD populations is also reviewed here. In terms of intellectual functioning, Taylor and colleagues found that children aged 1-18 with ASD of mixed intellectual functioning (both ID and no ID) who slept more, also had higher full-scale and verbal IQ scores, and that sleep duration, alongside parent-reported sleep apnoea symptoms, predicted performance IQ (PIQ; Taylor et al., 2012). Similarly, parent-reported total sleep disturbance scores were significantly correlated with non-verbal IQ scores in a small sample of school-age children (mean age = 10 years 7 months) with ASD (Gabriels, Cuccaro, Hill, Ivers, & Goldson, 2005). In contrast, several studies report no significant association between parent-reported total sleep disturbance scores and IQ scores (Hollway et al., 2013; May et al., 2015; Mayes & Calhoun, 2009). In terms of specific sleep problems and IQ, Hollway and colleagues found that children’s IQ scores were positively correlated with parent-reported sleep anxiety scores on the Children’s Sleep Habits Questionnaire (CSHQ) in a large sample of children aged 2-17 of mixed intellectual functioning, but not with CSHQ subscales measuring sleep duration or bedtime resistance (Hollway et al., 2013). In contrast, May et al. found that children’s FSIQ...
scores did not correlate with any subscales of the CSHQ in a sample of school-age children with ASD without ID (May et al., 2015). The conflicting findings reviewed above are hard to reconcile, particularly in light of the highly heterogeneous samples used between studies. These studies are also limited by the absence of objective measures with which to capture sleep. To date, only one known study has examined the relationship between objectively-measured sleep and IQ in children with ASD; finding that NREM C3 sleep spindle density was negatively associated with both full-scale and verbal IQ scores in a small sample of children with ASD without ID, whilst TD children showed distinct association between verbal IQ and other NREM EEG activity (Tessier, Lambert, Scherzer, Jemel, & Godbout, 2015).
### Table 2. Research exploring the relationship between sleep and cognition in preschool, school-age, and adolescent children with ASD

<table>
<thead>
<tr>
<th>Study</th>
<th>Age range (years)</th>
<th>Participants</th>
<th>ASD Cognitive Level</th>
<th>TD control group</th>
<th>Objective sleep measure</th>
<th>IQ &amp; Attention Area(s) Measured</th>
<th>Core finding regarding sleep and attention</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Tessier et al., 2015)</td>
<td>6-13</td>
<td>ASD (n=13)</td>
<td>No ID</td>
<td>✓</td>
<td>✓</td>
<td>FSIQ, PIQ, VIQ</td>
<td>FSIQ, VIQ &amp; PIQ correlated with different EEG sleep activity in children with ASD and TD children.</td>
</tr>
<tr>
<td>(May et al., 2015)</td>
<td>7-12</td>
<td>ASD (n=46)</td>
<td>No ID</td>
<td>✓</td>
<td>x</td>
<td>FSIQ</td>
<td>FSIQ scores were not associated with Time 1 or Time 2 total sleep disturbance scores or across any subscales of the CSHQ for the ASD group.</td>
</tr>
<tr>
<td>(Memari et al., 2013)</td>
<td>7-14</td>
<td>ASD (123)</td>
<td>No ID</td>
<td>x</td>
<td>x</td>
<td>Attention/EF</td>
<td>Children with lower parent-reported daily sleep time were more likely to demonstrated perseveration.</td>
</tr>
<tr>
<td>(Limoges et al., 2013)</td>
<td>16-27</td>
<td>ASD (n=17)</td>
<td>No ID</td>
<td>✓</td>
<td>✓</td>
<td>Attention, EF</td>
<td>Indicators of poor sleep correlated with selective attention.</td>
</tr>
<tr>
<td>(Hollway et al., 2013)</td>
<td>2-17</td>
<td>ASD (n=1583)</td>
<td>Mixed</td>
<td>x</td>
<td>x</td>
<td>FSIQ</td>
<td>IQ scores were positively correlated with parent-reported sleep anxiety but not sleep duration, bedtime resistance, or total sleep disturbance scores.</td>
</tr>
<tr>
<td>(Taylor et al., 2012)</td>
<td>1-18</td>
<td>ASD (n=335)</td>
<td>Mixed</td>
<td>x</td>
<td>x</td>
<td>FIQ, PIQ, VIQ</td>
<td>Children who slept fewer hours per night had lower FSIQ and verbal IQ scores. Parent-reported sleep duration, alongside parent-reported sleep apnoea symptoms, predicted performance IQ.</td>
</tr>
<tr>
<td>(Mayes &amp; Calhoun, 2009)</td>
<td>1-15</td>
<td>ASD (n=477)</td>
<td>Mixed</td>
<td>x</td>
<td>x</td>
<td>EF, PS, IQ</td>
<td>Overall sleep disturbance scores were not associated with IQ, working memory, or processing speed after controlling for autism severity. A significant association was seen between the ‘nightmares’ sleep disturbance score and IQ.</td>
</tr>
<tr>
<td>(Gabriels et al., 2005)</td>
<td>NS (M = 10 years 7 months)</td>
<td>ASD (n=14)</td>
<td>Mixed</td>
<td>x</td>
<td>x</td>
<td>NVIQ</td>
<td>Children in the lower NVIQ (NVIQ &lt; 56) group had more problems with sleep disturbance than children in the higher NVIQ (NVIQ &gt; 97) group. NVIQ scores were significantly correlated with sleep total scores.</td>
</tr>
</tbody>
</table>
ASD Autism Spectrum Disorder; CSHQ Children’s Sleep Habits Questionnaire; EF Executive Functioning; FSIQ Full-scale Intelligence Quotient; ID Intellectual Disability; IQ Intelligence Quotient; NS Not Stated; NVIQ Non-verbal Intelligence Quotient; PIQ Perceptual Intelligence Quotient; PS Processing Speed; TD Typically Developing; VIQ Verbal Intelligence Quotient.
2.6. Conclusion & future directions

ASD’s are a group of complex neurodevelopmental disorders which are further complicated by a high prevalence of attention problems and sleep difficulties. Despite high rates of co-morbid ADHD symptomology in this population, and a multitude of attention studies, much about the profile of cognitive attention in ASD remains unclear; with current research suggesting that children with ASD experience impairments in select attentional networks, but that these difficulties may only be evident at particular task levels. In terms of sleep research in ASD, the majority of previous studies conducted in paediatric ASD populations have focused primarily on assessing the prevalence and profile of sleep difficulties experienced by this population, rather than the impact these difficulties may be having on daytime attentional, intellectual, and behavioural functioning. The studies reviewed here allow us to draw some conclusions regarding the impact of sleep on neurobehavioural functioning in children with ASD. In terms of behaviour, previous research suggests a bi-directional relationship between sleep disturbance and autism symptomology, which is well validated by cross-sectional research utilising both subjective and objective sleep assessment measures (Goldman et al., 2009; 2011; Hoffman et al., 2005; Hollway et al., 2013; Mayes & Calhoun, 2009; Nadeau et al., 2015; Park et al., 2012; Schreck et al., 2004; Taylor et al., 2012; Tudor et al., 2012), and with preliminary support from longitudinal investigation (May et al., 2015). Similar bi-directional relationships are also observed between sleep disturbances and externalising behaviours of hyperactivity and aggression, although some inconsistencies between objective and subjective sleep measures in younger cohorts are noted. In addition, cross-sectional research suggests uni-directional relationships between reduced sleep quality and increased difficulty with impulsivity, oppositional, inattentive and adaptive functioning. Together these studies have identified clear relationships between overall sleep disturbance and a number of challenging behaviours in ASD, however, few studies to date have examined
the impact of sleep duration rather than sleep quality on behavioural functioning, or whether specific sleep difficulties may be impacting different areas of behavioural functioning; with most studies examining behaviour in regards to an overall parent-reported sleep disturbance composite score, or through the division of children into either “good” and “poor” sleeper groups. Given that children with ASD are known to experience the full spectrum of sleep difficulties, and specific treatment approaches are known to be more efficacious for certain sleep problems over others (e.g. pharmacological melatonin treatment for sleep onset difficulties), identifying which aspects of sleep are also affecting specific behavioural outcomes is likely to highlight the most important area/s for focus in terms of the development and application of sleep interventions. In addition to these gaps in the literature, only two studies to date have examined the relationship between sleep and behavioural functioning longitudinally (May et al. 2015; Anders et al. 2012), with the majority of studies instead employing a cross-sectional design within populations which span preschool to adolescence age ranges, and encompass children both with and without comorbid intellectual disability. Whilst cross-sectional research has suggested that different age-groups may experience different sleep problems (Goldman et al., 2012), the paucity of longitudinal sleep research conducted in children with ASD means that little is currently known regarding the developmental trajectory of sleep problems in this population, let alone the relative impact age may have on the relationship between sleep and behavioural functioning. Future research would significantly add to the literature in this area by examining the relationship between these constructs within more restricted age and cognitive IQ bands, and through longitudinal follow-up of these children over time. In terms of attention and intellectual functioning, The research reviewed here generally supports a relationship between aspects of both macro and micro sleep architecture and cognitive attention/executive functioning and overall intellectual functioning in children with ASD, whilst also clearly highlighting the sparsity of previous
studies conducted in this area to date. The finding of unique associations between EEG sleep activity and areas of cognitive processing in ASD is interesting, and suggests that children with ASD may be using different sleep-related brain networks to TD children to process information while asleep; which may be driven by a unique cortical organisation in this population. Inconsistencies between studies, particularly in regards to the relationship between sleep and intellectual functioning, are further complicated by the inclusion/exclusion of comorbid intellectual disability between studies, and predominant reliance on subjective sleep measures to capture sleep, however, together suggest that targeted sleep interventions may also offer a new approach to improve cognitive functioning, across these domains, in these children. Further research into the relationship between sleep and all areas of cognition is clearly warranted, however, a particular emphasis is placed on further examination of the relationship between sleep and cognitive attention functioning in this population; with attention considered the building block upon which all other cognitive functions rest. Attentional processes appear to be particularly sensitive to general reductions in sleep quality such as sleep onset latency problems and reduced sleep efficiency (Forest & Godbout, 2005), which are common sleep concerns in children with ASD. In addition, as the current review has demonstrated children with ASD have been shown also experience increased difficulties in several areas of cognitive attention. Despite these links, only two previous studies have examined the impact of sleep on higher-order attention/EF problems in children with ASD; with parent-reported sleep quantity but not sleep quality found to be associated with performance (Mayes & Calhoun, 2009; Memari et al., 2013). Future research utilising both objective and subjective sleep measures, and objective assessments of both lower and higher-order attentional constructs, is clearly warranted in order to further investigate the impact of sleep disruption on attentional processing in this population.
References


Declaration by candidate

In the case of Chapter 3, the nature and extent of my contribution to the work was the following:

<table>
<thead>
<tr>
<th>Nature of contribution</th>
<th>Extent of contribution (%)</th>
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<tbody>
<tr>
<td>Study design, data collection, data analysis, interpretation of results, preparation of manuscript</td>
<td>45</td>
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</tbody>
</table>

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

<table>
<thead>
<tr>
<th>Name</th>
<th>Nature of contribution</th>
<th>Extent of contribution (%) for student co-authors only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ms. F. Fletcher</td>
<td>Study design, data collection, data analysis, interpretation of results, preparation of manuscript</td>
<td>45</td>
</tr>
<tr>
<td>Dr R. Conduit</td>
<td>Study design, interpretation of results, feedback on prepared manuscript</td>
<td></td>
</tr>
<tr>
<td>Prof N. Rinehart</td>
<td>Study design, interpretation of results, feedback on prepared manuscript</td>
<td></td>
</tr>
<tr>
<td>Prof S. Rajaratnam</td>
<td>Study design, feedback on prepared manuscript</td>
<td></td>
</tr>
<tr>
<td>Dr H. Heussler</td>
<td>Study design, feedback on prepared manuscript</td>
<td></td>
</tr>
<tr>
<td>Prof K. Cornish</td>
<td>Study design, interpretation of results, feedback on prepared manuscript</td>
<td></td>
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</table>

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate’s and co-authors’ contributions to this work.

<table>
<thead>
<tr>
<th>Candidate’s Signature</th>
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<th>Main Supervisor’s Signature</th>
<th>Date</th>
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CHAPTER 3

PROFILING SLEEP IN SCHOOL-AGE CHILDREN WITH AUTISM SPECTRUM DISORDER

Preamble to Paper 1

Examination of previous research conducted in children with Autism Spectrum Disorder (ASD) has revealed an over-reliance on subjective parent-report sleep measures to define the sleep difficulties experienced by this population. The focus of Paper 1 was, therefore, to assess and profile differences between school-age children with ASD without intellectual disability (ID), and their typically-developing (TD) peers, using a multi-modal (objective and subjective) sleep assessment method. The current paper is only the second study to utilise actigraphy to specifically assess differences between school-age children with ASD without ID and TD children’s sleep-wake profiles. In addition, it further builds on previous research by examining concordance between actigraphy and the Children’s Sleep Habits Questionnaire, and through exploration of age-related changes in children’s objective and subjective sleep profiles.


Note: This paper has been accepted with revisions in the Journal of Autism and Developmental Disorders

Abstract

The current study explored differences in the sleep-wake profiles of 34 school-aged children with Autism Spectrum Disorder (ASD) without intellectual disability, and 34 age-and-gender-matched typically-developing (TD) children; using fourteen nights of actigraphy and the Children’s Sleep Habits Questionnaire. Poorer parent-reported sleep quality and longer actigraphy-derived sleep onset latencies were observed among children with ASD. Parent-reported concerns regarding sleep initiation were supported by actigraphy, and parent-reported bedtime resistance was associated with a later time of sleep onset in both groups, and a shorter total sleep time in children with ASD. These findings reinforce difficulties in sleep initiation in children with ASD, whilst highlighting the benefits of combining parent-report with objective sleep measurement.

Keywords: Autism Spectrum Disorder, Sleep problems, Insomnia, school-aged children, Actigraphy
Autism Spectrum Disorder (ASD) is a complex and life-long neurodevelopmental condition which affects around 62 in every 10,000 children worldwide (Elsabbagh et al., 2012). Autistic Disorder and Asperger’s Disorder were previously classified as two discrete disorders, originally introduced under the category of ‘Pervasive Developmental Disorder’ in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; American Psychiatric Association, 2000), and now encompassed under the single diagnostic term ASD (DSM-V; American Psychiatric Association, 2013). ASD is characterised by impairments in social and communicative functioning, along with stereotyped and repetitive behaviour (American Psychiatric Association, 2013). Research has also indicated that children with ASD experience sleep problems at a disproportionately high rate, with standardised screening questionnaires reporting rates of 66% to 82% in children with ASD compared to 26% to 50% in Typically Developing (TD) children (Couturier et al., 2005; Hodge, Carollo, Lewin, Hoffman, & Sweeney, 2014; Souders et al., 2009).

The school-aged years are a critical period where the pathways to a child’s lifetime social, emotional and educational outcomes begin. The types of sleep problems experienced by school-aged children with ASD are wide-ranging and include insomnia (Liu, Hubbard, Fabes, & Adam, 2006; Schreck & Mulick, 2000; Wiggs & Stores, 2004; Williams, Sears, & Allard, 2004), parasomnias and sleep-related anxiety (Couturier et al., 2005; Hodge et al., 2014; Hoffman, Sweeney, Gilliam, & Lopez-Wagner, 2006; Paavonen et al., 2008; Schreck & Mulick, 2000), sleep-related breathing and movement disorders (Liu et al., 2006; Schreck & Mulick, 2000; Williams et al., 2004), and hypersomnia (Liu et al., 2006; Williams et al., 2004). Of these, insomnia is the most commonly reported sleep problem (Malow et al., 2006), as characterised in children with ASD by a longer sleep onset latency (SOL) and more frequent and/or longer nocturnal awakenings than TD peers (Allik, Larsson, & Smedje, 2006; Couturier et al., 2005; Hodge et al., 2014; Hoffman et al., 2006; Honomichl, Goodlin-Jones,
Burnham, Gaylor, & Anders, 2002; Krakowiak, Goodlin-Jones, Hertz-Picciotto, Croen, & Hansen, 2008; Paavonen et al., 2008; Souders et al., 2009). In addition, discrepant trajectories in parent-reported sleep problems have been found between children with and without ASD; with difficulties in several sleep areas (e.g., bedtime resistance, sleep anxiety, and night wakings) peaking in middle childhood in children with ASD (Hodge et al., 2014; Hoffman et al., 2006; May, Cornish, Conduit, Rajaratnam, & Rinehart, 2015). An examination of developmental changes using objective sleep measurement, however, revealed a similar developmental trajectory in children with and without ASD, across both sleep timing and sleep duration. However, group differences in SOL were more pronounced at baseline than at follow-up, 2-3 years later (Allik, Larsson, & Smedje, 2008).

Polysomnography (PSG) is considered the gold standard for the assessment of sleep. Few studies have utilised PSG in children with ASD however, as the procedures involved are often not tolerated in this population due to the novelty of the sleep environment and associated stress and anxiety. Sleep data collected through PSG may therefore not accurately reflect the typical sleep experience in children with ASD (Hodge, Parnell, Hoffman, & Sweeney, 2012). In addition, PSG is not indicated for the routine evaluation of insomnia (Sateia, Doghramji, Hauri, & Morin, 2000; Schutte-Rodin, Broch, Buysse, Dorsey, & Sateia, 2008) or circadian rhythm disorders (Morgenthaler et al., 2007), both of which are common sleep concerns in children with ASD. The majority of studies examining the profile of sleep in early school-aged children with ASD have instead done so using subjective parental reports; with the Children’s Sleep Habits Questionnaire (Owens, Spirito, & McGuinn, 2000) the most commonly used standardised measure. Given that sleep difficulties are also reported to commonly occur in school-age children without developmental difficulties (Owens, 2007), the inclusion of a TD control group is considered essential in order to map out the unique profile and trajectory of sleep in children with ASD; with a number of recent studies utilising
the CSHQ to examine sleep differences between children with ASD and TD controls (Couturier et al., 2005; Giannotti et al., 2008; Giannotti, Cortesi, Cerquiglini, Vagnoni, & Valente, 2011; Hodge et al., 2014; Hoffman et al., 2006; May et al., 2015; Souders et al., 2009).

Comparative to PSG, actigraphy is a less invasive means to objectively measure the sleep-wake cycle in children with ASD, within their home environment. Few studies to date have specifically aimed to use actigraphy to assess sleep-wake differences between school-aged children with ASD and their TD peers (Allik et al., 2006; Souders et al., 2009); and only one has examined these difficulties in children with ASD without intellectual disability (ID; Allik et al., 2006). Both studies reported increased SOL in children with ASD compared to TD controls. Additionally, neither study found a significant difference in the number or duration of long wake episodes (i.e., >5 minutes). Discrepant findings were found regarding the quality of sleep, however, whereby significantly lower sleep efficiency (SE) was reported in children aged 8 to 12 years with ASD without ID (Allik et al., 2006), but not in children aged 4 to 10 years with ASD, across varied levels of developmental disability (Souders et al., 2009). These discrepant findings are hard to reconcile due to the heterogeneity of the ASD samples (high-functioning individuals versus varied levels of developmental disability), and inconsistencies in operational definitions, experimental procedures and methodology. In addition, while previous research has examined how the CSHQ compares to actigraphy in TD and other clinical populations (Alfano, Patriquin, & De Los Reyes, 2015; Holley, Hill, & Stevenson, 2010), no known study has examined the concordance between subscales from the CSHQ and actigraphy in children with ASD. Combining these two methods of sleep measurement would also allow full capture of children’s sleep profiles; with the CSHQ able to provide information regarding environmental and behavioural aspects of sleep immeasurable via objective methods, and actigraphy providing a more reliable measure of
children’s sleep onset and night wakings (Tikotzky & Sadeh, 2001; Wiggs, Montgomery, & Stores, 2005).

In the current study, our goal was, therefore, to explore differences in the sleep-wake profile between school-aged children with and without ASD, without ID; using a combination of both objective and standardised parent-report measures. The first aim of the study was to compare parent-reported sleep problems (via the CSHQ) and objectively measured sleep profiles (via two weeks of actigraphy), in children with and without ASD. We hypothesised that children with ASD would have significantly higher scores on the CSHQ than TD children, accompanied by a significantly longer actigraphy-derived SOL and lower sleep efficiency. Our second aim was to examine cross-sectional changes in subjective and objective sleep profiles, across the school-aged years. From the CSHQ, it was hypothesised that younger children with ASD (6-8 years) would have greater parent-reported sleep problems than older children with ASD (9-12 years). From actigraphy, it was hypothesised that children with and without ASD would have comparable cross-sectional changes in sleep; including a later sleep onset time and shorter sleep duration in older children (9-12 years) compared to younger children (6-8 years). Finally, we aimed to examine the correspondence between actigraphy and the CSHQ; including both direct (i.e., sleep duration, night wakings, and sleep onset delay subscales) and indirect (e.g., sleep anxiety, bedtime resistance subscales) comparisons.

Methods

Participants

A total of 68 children participated in this study. All children were aged between 6;0-12;11 years and had a full-scale intelligence quotient (FSIQ) above 70. Children were excluded if they had any parent-reported history of sleep disordered breathing (SDB) or
restless leg syndrome, diagnosed seizure disorder, or any medical conditions that significantly impacted hearing, vision, or motor control.

**ASD Group**

A total of 34 children with ASD (age range 6;0-12;10 years) were recruited from the community through a variety of services for children with ASD in and around Melbourne including; AMAZE, the Asperger Syndrome Support Network Victoria, speech therapists, parent support groups, Melbourne Children’s Clinic, and via online advertisements. All children in the ASD group were tested between August 2012 and August 2013 and had a clinical diagnosis of Autistic Disorder, Asperger’s Disorder, or ASD. Clinical diagnoses were based on comprehensive multidisciplinary diagnostic assessments performed by clinicians at child paediatric or psychology clinics, and completely independent from the current research project. Diagnostic reports, completed by either a paediatrician or registered psychologist, were obtained for each child in the ASD group and checked against the DSM-IV-TR symptom checklist to ensure criteria was met.

**Typically developing Group**

A total of 34 children (age range 6;0-12;6 years) were drawn from a larger sample of 75 children tested between July 2012 and May 2014 from the Monash University Networks of Attention and Paediatric Sleep (NAPS) project. TD children were recruited through the distribution of information through local Primary Schools, community centres, Melbourne-based print media, and via online advertisements. Children were considered for matching purposes if they were without a current or previous diagnosis of any neuropsychiatric disorder, obtained a T-score below 75 on the Social Responsiveness Scale (SRS; Constantino
& Gruber, 2005), did not have a sibling with a diagnosis of ASD, were tested outside of school holidays, and had at least 11 nights of actigraphy and corresponding sleep diary data.

**Measures**

*Demographics and Medical History*

Demographic information (gender, age) and medical history (medication, medical problems, formal diagnoses, history of sleep difficulties, and history of learning difficulties/language delays) were obtained from parents using a semi-structured interview during initial screening and via diagnostic reports. Socio-economic information including child ethnicity and parent education were obtained using a brief questionnaire. A socioeconomic status (SES) score, indicating relative socio-economic advantage/disadvantage, was calculated for each participant based on their residential postcode using the Socio-economic Indexes for Areas data from the Australian Bureau of Statistics which allocates each area a decile number ranging from 1 to 10 where 1 indicates the most disadvantaged, and 10 indicates the most advantaged area (Australian Bureau of Statistics, 2013).

*Intellectual Functioning*

The two-subtest version (vocabulary and matrix reasoning) of the Wechsler Abbreviated Scale of Intelligence which yields an FSIQ, was completed for all children (WASI; Wechsler, 1999). The WASI is a short and reliable measure of intelligence, suitable for use with individuals aged 6-89 years. The WASI FSIQ is comparable to the Wechsler Intelligence Scale for Children – Third Edition (WISC-III; Wechsler, 1991) FSIQ, and intercorrelations between FSIQ scores derived from the two and four subtest versions of the WASI range from .91 to .97 (Wechsler, 1999).
Autistic Symptoms

The Social Responsiveness Scale (SRS) is a 65-item parent-completed rating scale, designed to measure social impairment associated with ASD in children aged 4 to 18 years (Constantino & Gruber, 2005). Items are rated on a four-point Likert scale where 1 is “not true” and 4 is “almost always true,” based on the child’s behaviour during the previous six months. The questionnaire yields a total score (ranging from 0 to 195), which can be converted to a T-score and provides an indicator of severity of social impairment. T-scores $\geq 75$ have been found to discriminate children with and without ASD with specificity and sensitivity values of .75 and .85, respectively (Constantino et al., 2003). Correlations between SRS scores and Autism Diagnostic Interview-Revised domain scores range from .65 to .77 (Constantino et al., 2003).

Sleep Measures

The Children’s Sleep Habits Questionnaire (CSHQ) is a caregiver-completed, 48-item questionnaire designed to examine sleep behaviour in children aged 4 to 10 years (Owens et al., 2000). Although the CSHQ has not been normed in children above 10 years of age, a number of previous studies have utilised it to assess sleep in older children with ASD and their TD peers (Couturier et al., 2005; Hodge et al., 2014; Hoffman et al., 2006; May et al., 2015). The questionnaire yields a total score, and 8 subscale scores relating to sleep complaints commonly found to affect this age group: bedtime resistance; delay of sleep-onset; duration of sleep; sleep anxiety; night wakings; parasomnias; sleep-disordered breathing; and daytime sleepiness. Parents are asked to rate each item on a three-point scale according to how frequently that behaviour occurs in a “recent typical week” where 3 is ‘usually’ and 1 is ‘rarely.’ A cut-off score of 41 on the CSHQ can be utilised to screen for sleep disturbance with a sensitivity of 0.80 and specificity of 0.72 (Owens et al., 2000).
Cronbach’s alpha for CSHQ subscales ranged from .40 to .80, in children with ASD (Johnson, Turner, Foldes, Malow, & Wiggs, 2012).

All children wore an Actiwatch-2 (Respironics, USA), a wristwatch-like device with a self-contained micro-computer (16g), on their non-dominant wrist for 14-15 nights. Each actiwatch contains a marker button (located on the side of the watch), an integrated light sensor (range 400-900 nm), and a solid state piezo-electric accelerometer with a sampling rate of 32 Hz and a non-volatile memory of 1Mbit. Each actiwatch was configured to record at 30s epochs and data was subsequently analysed at a medium sensitivity threshold (i.e., 40 activity counts per epoch required to be scored as ‘wake’). These settings have been validated against PSG, providing an agreement rate of 87.3%, sensitivity of 93.9% and a specificity of 59.0% (note that despite the low specificity, overall wake time was not significantly different to PSG wake time) for PSG total sleep, wake times, and sleep efficiency (Hyde et al., 2007). A ten-minute immobility rule was applied for the scoring of sleep onset time, recently cited as the most appropriate for the use of the Actiwatch-2 in school-aged children (Meltzer, Walsh, & Peightal, 2015). Children and parents were instructed to press the marker button to indicate bedtime and get-up time. Marker button presses, activity counts per epoch, and light information were stored in the actiwatch memory and later downloaded to the Respironics Actiware Software (Version 5.70.1). Bedtime and get-up time were manually scored in accordance with marker button presses in conjunction with parental sleep diaries (Meltzer, Montgomery-Downs, Insana, & Walsh, 2012). As the most widely used definition for nocturnal wake frequency, night wakings (NW) were manually scored as 10 or more consecutive epochs (i.e., 5 minutes) of wake in between sleep-onset time and sleep-offset time (Meltzer et al., 2012). Five additional actigraphy variables were autoscored by the Respironics software which covered timing, sleep duration, sleep initiation, and overall sleep efficiency (see Table 1).
Table 1. Actigraphy Variables and coding definitions

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedtime</td>
<td>Clock time attempted to fall asleep as indicated by event marker and sleep</td>
</tr>
<tr>
<td></td>
<td>diary</td>
</tr>
<tr>
<td>Get-up Time</td>
<td>Clock time of get-up time as indicated by event marker and sleep diary</td>
</tr>
<tr>
<td>Sleep-onset Time</td>
<td>Clock time of the first epoch after ‘Bedtime’ followed by 10 consecutive</td>
</tr>
<tr>
<td></td>
<td>minutes of immobility</td>
</tr>
<tr>
<td>Sleep-offset Time</td>
<td>Clock time of the last epoch of ten consecutive minutes of immobility</td>
</tr>
<tr>
<td></td>
<td>before ‘Get Up Time’</td>
</tr>
<tr>
<td>Total Sleep Time</td>
<td>Duration (in minutes) between sleep onset and sleep offset, minus total</td>
</tr>
<tr>
<td></td>
<td>duration of nocturnal awakenings</td>
</tr>
<tr>
<td>Sleep Onset latency</td>
<td>Time (in minutes) between ‘Bedtime’ and ‘Sleep Onset Time’</td>
</tr>
<tr>
<td>Night Wakings</td>
<td>Total duration (in minutes) and number of nocturnal awakenings ≥ 5 minutes</td>
</tr>
<tr>
<td>Sleep Efficiency</td>
<td>Total sleep time divided by time in bed (%)</td>
</tr>
</tbody>
</table>

Parents were also asked to maintain a sleep-wake diary throughout their child’s participation. Parents indicated bedtime, time of sleep onset, time and duration of night awakenings, time of sleep offset, get-up time, daytime naps, and any time the actiwatch was removed. If a parent indicated that the child had an unusual night of sleep (e.g., sleepover, illness) this night was excluded from analysis.

Procedure

The current study received approval by the Monash University Ethics Committee. Upon initial contact by the parent or guardian, screening was conducted in order to determine whether the child met eligibility criteria. Children and parents were seen on two occasions, 14-15 days apart, within either the participant’s home or at Monash University. The first session consisted of obtaining informed written consent from parents, the distribution of
relevant paperwork and actiwatches, and administration of the WASI. Both parents and children were instructed in the use of the Actiwatch-2, when to remove the watch (before immersion in water), and when to press the marker button.

Data Analyses

All analyses were performed using SPSS, version 22 for Windows (IBM Corp, 2013). The data set was assessed for univariate outliers within groups using z-scores. Any z-scores greater than ±3.29 were transformed to one value higher than the next highest/lowest non-outlier in order to reduce their influence (Howell, 2007). χ² analysis was used for categorical data generated from semi-structured screening interview (e.g., global sleep question), and CSHQ total cut-off. Comparisons between the ASD and TD groups were accomplished using T-tests, two-way ANOVAs, and Mann-Whitney U tests. Effect sizes for the two-way ANOVAs were based on η², where values ≥.01 indicate a small effect size, values ≥.06 indicate a medium effect size and values ≥.14 indicate a large effect size. Finally, a series of partial spearman correlations were performed between the CSHQ subscales and actigraphy parameters, controlling for age.

Results

Participant Characteristics

Participant characteristics are reported in Table 2. Participants in the ASD and TD groups were matched pairwise for gender (23 males, 11 females) and group-matched for chronological age. Average FSIQ was significantly higher in the TD group than the ASD group, \( t (66) = 4.15, p < .001 \), and the ethnicity of the sample was predominantly Caucasian. SES scores did not differ significantly between groups, \( t (66) = 0.57, p = .57 \), and an undergraduate degree was the most frequent parental education level across both groups.
Table 2. Participant characteristics; reported as M (SD) or n (%)

<table>
<thead>
<tr>
<th></th>
<th>ASD (n = 34)</th>
<th>TD (n = 34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>106.65 (24.49)</td>
<td>104.68 (19.97)</td>
</tr>
<tr>
<td>FSIQ</td>
<td>99.53 (13.87)</td>
<td>112.97 (12.81)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>32 (94.1)</td>
<td>30 (88.2)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (5.9)</td>
<td>4 (11.8)</td>
</tr>
<tr>
<td>SES Score</td>
<td>7.71 (2.14)</td>
<td>7.35 (2.91)</td>
</tr>
<tr>
<td>Primary Caregiver Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial High school</td>
<td>3 (8.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Completed High School</td>
<td>5 (14.7)</td>
<td>2 (5.9)</td>
</tr>
<tr>
<td>Undergraduate Degree</td>
<td>21 (61.8)</td>
<td>20 (58.8)</td>
</tr>
<tr>
<td>Postgraduate Degree</td>
<td>4 (11.8)</td>
<td>10 (29.4)</td>
</tr>
<tr>
<td>Not Specified</td>
<td>1 (2.9)</td>
<td>2 (5.9)</td>
</tr>
</tbody>
</table>

Regarding medication use, 17 children in the ASD group were currently taking prescription medication, and 6 of these children were taking two or more medications. Medications within the ASD group included: melatonin (20.6%), Selective-Serotonin Reuptake Inhibitors (SSRI’s; 11.8%), stimulant medication (8.8%), anticonvulsants (2.9%), atypical antipsychotics (5.9%), Clonidine (8.8%), and Atomoxetine (2.9%). No TD children were taking psychotropic medication. Asthma medications were equally as prevalent in the TD and ASD group (8.8%).

Parent-reported sleep profiles

The number of parents to report a history of sleep problems in response to the single-item screening question (i.e., “Has your child had issues with sleep or a previous history of sleep difficulties?”) was significantly higher in the ASD group (82.4%) compared to the TD group (29.4%), $\chi^2(1,N=68) = 19.34, p < .001$. The percentage of parents to report current
sleep problems according to the CSHQ (i.e., total score ≥41) was also significantly higher in the ASD group (91.2%) compared to the TD group (50.0%), \( \chi^2 (1, N = 68) = 13.88, p <.001 \). Additionally, two-way ANOVAs identified significant main effects of group for CHSQ total scores and all CSHQ subscales, whereby the ASD group had a significantly greater severity of parent-reported sleep disturbance than the TD group (see Table 3).

Two significant main effects for age were also observed; with decreased bedtime resistance and sleep anxiety in older children (see Table 3). In addition, significant interaction effects were identified between group and age for CSHQ total scores, bedtime resistance and daytime sleepiness; whereby group differences were greater in the 6-8 age group than the 9-12 age group (see Figure 1).

Figure 1. Significant interaction effects between age group and diagnostic group, for Children’s Sleep Habits Questionnaire (CSHQ) total score, bedtime resistance subscale and daytime sleepiness subscale
## Table 3. Two-Way ANOVAs to identify main effects for group and age, and interaction effects for the Children’s Sleep Habits Questionnaire (CSHQ) and actigraphy

<table>
<thead>
<tr>
<th></th>
<th>TD Group</th>
<th>ASD Group</th>
<th></th>
<th></th>
<th></th>
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<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6-8 yrs</td>
<td>9-12 yrs</td>
<td>6-8 yrs</td>
<td>9-12 yrs</td>
<td>Group</td>
<td>Age</td>
<td>Interaction</td>
<td>Interaction</td>
</tr>
<tr>
<td></td>
<td>(n = 20)</td>
<td>(n = 14)</td>
<td>(n = 20)</td>
<td>(n = 14)</td>
<td>F value</td>
<td>η²_p</td>
<td>F value</td>
<td>η²_p</td>
</tr>
<tr>
<td>CSHQ Total Score</td>
<td>41.90 (7.43)</td>
<td>43.21 (8.84)</td>
<td>55.40 (10.56)</td>
<td>48.14 (6.87)</td>
<td>18.63 ***</td>
<td>.23</td>
<td>1.94</td>
<td>.03</td>
</tr>
<tr>
<td>Bedtime Resistance</td>
<td>7.50 (2.04)</td>
<td>6.79 (1.12)</td>
<td>9.95 (3.32)</td>
<td>6.79 (1.19)</td>
<td>4.90 *</td>
<td>.07</td>
<td>12.29 ***</td>
<td>.16</td>
</tr>
<tr>
<td>Sleep Onset Delay</td>
<td>1.40 (0.68)</td>
<td>1.86 (0.86)</td>
<td>2.05 (0.89)</td>
<td>2.00 (0.78)</td>
<td>4.00 *</td>
<td>.06</td>
<td>1.05</td>
<td>.02</td>
</tr>
<tr>
<td>Sleep Duration</td>
<td>3.95 (1.45)</td>
<td>4.29 (1.68)</td>
<td>5.75 (1.86)</td>
<td>5.57 (1.70)</td>
<td>13.86 ***</td>
<td>.18</td>
<td>.04</td>
<td>.00</td>
</tr>
<tr>
<td>Sleep Anxiety</td>
<td>5.55 (1.67)</td>
<td>4.79 (1.19)</td>
<td>7.30 (2.16)</td>
<td>5.93 (1.69)</td>
<td>11.23***</td>
<td>.15</td>
<td>6.12 *</td>
<td>.09</td>
</tr>
<tr>
<td>Night Wakings</td>
<td>3.95 (1.19)</td>
<td>3.50 (0.94)</td>
<td>5.15 (1.79)</td>
<td>4.71 (1.33)</td>
<td>12.61 ***</td>
<td>.17</td>
<td>1.70</td>
<td>.03</td>
</tr>
<tr>
<td>Parasomnias</td>
<td>8.60 (1.73)</td>
<td>8.86 (1.61)</td>
<td>10.70 (2.87)</td>
<td>9.57 (1.56)</td>
<td>7.50 **</td>
<td>.11</td>
<td>.72</td>
<td>.01</td>
</tr>
<tr>
<td>SDB</td>
<td>3.10 (0.31)</td>
<td>3.29 (0.61)</td>
<td>3.70 (0.98)</td>
<td>3.57 (0.94)</td>
<td>5.70 *</td>
<td>.08</td>
<td>0.02</td>
<td>.00</td>
</tr>
<tr>
<td>Daytime Sleepiness</td>
<td>10.40 (2.64)</td>
<td>12.00 (3.92)</td>
<td>14.50 (3.04)</td>
<td>12.50 (4.01)</td>
<td>7.77 **</td>
<td>.11</td>
<td>0.06</td>
<td>.00</td>
</tr>
</tbody>
</table>

### Actigraphy

<p>| | | | | | | | |</p>
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<thead>
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<tbody>
<tr>
<td></td>
<td>6-8 yrs</td>
<td>9-12 yrs</td>
<td>6-8 yrs</td>
<td>9-12 yrs</td>
<td>Group</td>
<td>Age</td>
<td>Interaction</td>
</tr>
<tr>
<td></td>
<td>(n = 20)</td>
<td>(n = 14)</td>
<td>(n = 20)</td>
<td>(n = 14)</td>
<td>F value</td>
<td>η²_p</td>
<td>F value</td>
</tr>
<tr>
<td>Bedtime</td>
<td>21:01 (0:44)</td>
<td>21:47 (0:54)</td>
<td>20:45 (0:33)</td>
<td>21:02 (0:35)</td>
<td>8.30 **</td>
<td>.12</td>
<td>8.93 **</td>
</tr>
<tr>
<td>Get up time</td>
<td>7:21 (0:37)</td>
<td>7:37 (0:39)</td>
<td>7:23 (0:41)</td>
<td>7:22 (0:33)</td>
<td>0.44</td>
<td>.01</td>
<td>0.56</td>
</tr>
<tr>
<td>Sleep onset time</td>
<td>21:13 (0:37)</td>
<td>22:12 (1:00)</td>
<td>21:13 (0:37)</td>
<td>21:33 (0:42)</td>
<td>2.97</td>
<td>.05</td>
<td>11.95 ***</td>
</tr>
<tr>
<td>Sleep offset time</td>
<td>6:55 (0:41)</td>
<td>7:20 (0:44)</td>
<td>6:56 (0:42)</td>
<td>6:58 (0:33)</td>
<td>1.10</td>
<td>.02</td>
<td>1.88</td>
</tr>
<tr>
<td>TST</td>
<td>561.13 (29.77)</td>
<td>542.37 (31.46)</td>
<td>567.45 (30.28)</td>
<td>535.64 (41.52)</td>
<td>0.00</td>
<td>.00</td>
<td>9.43 **</td>
</tr>
<tr>
<td>SOL</td>
<td>21.69 (10.61)</td>
<td>25.47 (11.32)</td>
<td>31.55 (19.08)</td>
<td>39.83 (32.44)</td>
<td>6.13 *</td>
<td>.09</td>
<td>1.52</td>
</tr>
<tr>
<td>NW (duration)</td>
<td>8.78 (4.79)</td>
<td>5.87 (5.94)</td>
<td>9.12 (8.50)</td>
<td>7.83 (6.16)</td>
<td>0.49</td>
<td>.01</td>
<td>1.65</td>
</tr>
<tr>
<td>NW (number)</td>
<td>1.25 (0.77)</td>
<td>0.86 (0.88)</td>
<td>1.10 (0.81)</td>
<td>0.91 (0.66)</td>
<td>.06</td>
<td>.00</td>
<td>2.27</td>
</tr>
<tr>
<td>SE</td>
<td>90.89 (3.05)</td>
<td>91.90 (2.20)</td>
<td>89.32 (3.69)</td>
<td>88.13 (5.11)</td>
<td>8.71 **</td>
<td>.12</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**Note.** ASD: Autism Spectrum Disorder; CSHQ: Children’s Sleep Habits Questionnaire; NW: night wakings; SDB: sleep disordered breathing; SE: sleep efficiency; SOL: sleep onset latency; SOffT: sleep offset time; SOT: sleep onset time; TD: Typically-developing, TST: total sleep time. p ≤.05. **p ≤.01. ***p ≤.001
Actigraphy derived sleep profiles

During data collection, one child in the ASD group was unable to tolerate the actiwatch. As a result, this participant and their corresponding TD gender match were removed from subsequent analyses. Significant main effects for group were observed for bedtime, sleep onset latency (SOL) and sleep efficiency (SE), with the ASD group characterised by an earlier bedtime, longer SOL, and decreased SE (see Table 3). However, after controlling for SOL, a two-way ANCOVA found there was no longer a significant main effect for group on SE, $F(1, 61) = 2.32, p = .13$. Importantly, after controlling for bedtime using a second two-way ANCOVA, the significant main effect for group on average SOL remained, $F(1, 61) = 8.21, p = .006$.

Three significant main effects for age were observed, with a significantly later bedtime, sleep-onset time and decreased total sleep time (TST) in the older age group. No significant interaction effects were observed for any actigraphy variables (see Table 3).

Figure 2. Within-child standard deviations for actigraphy-derived sleep onset latency (SOL SD) for the Autism Spectrum Disorder (ASD) and Typically Developing (TD) groups. Each dot represents a single participant.  
Note: Mean within-child ‘SOL SD’ for each group is denoted by the solid line (i.e., 19.44 in the ASD group and 12.81 in the TD group)
In addition to the main effect of group on average SOL, also of note is the increased between-child variation in the ASD group compared to the TD group, as demonstrated by larger group SDs (see Table 3). Within-child variation was also captured by individual participant standard deviations across the fourteen nights of data collection. An additional two-way ANOVA was performed to demonstrate a significant main effect for group on the variability of SOL \( F(1, 62) = 8.08, p = .006 \), whereby within-child variability was greater in the ASD group (M = 19.44, SD = 9.86) than the TD group (M = 12.81, SD = 7.74) (see Figure 2). No significant age \( F(1, 62) = 0.01, p = .92 \) or interaction \( F(1, 62) = 0.72, p = .40 \) effects were observed.

**Effect of sleep medication on sleep profiles**

Sleep profiles were explored further within the ASD group between those who were (\( n = 7 \)), and were not (\( n = 26 \)), taking medication to aid sleep. No significant differences were observed in parent-reported sleep disturbance according to CSHQ total scores \( U = 84.50, p = .68 \), or in actigraphic get-up time \( U = 64.00, p = .25 \), TST \( U = 65.00, p = .27 \), SOL \( U = 55.00, p = .12 \), NW \( U = 85.00, p = .81 \), or SE \( U = 55.00, p = .12 \). However, there was a significant difference in actigraphic bedtime \( U = 37.50, p = .016 \) and sleep-onset time, \( U = 35.50, p = .012 \), whereby sleep-medicated children went to bed significantly earlier, and fell asleep earlier, than non-sleep medicated children. The subsequent removal of the sleep medicated children from the ASD group reduced the difference (between the TD and ASD group) in bedtime from 29 minutes to 23 minutes \( F(1, 55) = 4.21, p = .045 \), and the difference in sleep-onset time decreased from 17 minutes to 7 minutes \( F(1, 55) = .62, p = .43 \).
Correspondence between the CSHQ and Actigraphy

Partial correlations (controlling for chronological age) between actigraphy variables and comparable CSHQ subscales (i.e., night waking, sleep onset delay, sleep duration) are displayed in Table 4. First, there were no significant correlations between the night wakings subscale of the CSHQ and any actigraphy parameters, across either the TD or the ASD group. Second, there were no significant correlations between the sleep duration subscale and the corresponding actigraphy variables (i.e., TST). The sleep duration subscale was significantly correlated with morning sleep schedules, however, such that increased parental concern was associated with a later time of sleep offset in both groups, and later get up time in the ASD group. Third, for the sleep onset delay subscale, a number of significant relationships were identified in children with ASD, with higher scores associated with longer SOL, later bed time/sleep onset time, lower sleep efficiency and shorter TST. For TD children, however, this subscale was associated only with a later bed time, and a later sleep offset time/get up time.
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*p ≤ .05, ** p ≤ .01, TD: Typically-developing, CSHQ: Children’s Sleep Habits Questionnaire, SDB: sleep disordered breathing, SOT: Sleep Onset Time, SOFFT: Sleep offset time, TST: Total sleep time (minutes), SOL: sleep onset latency (minutes), NW: Duration of Night Wakings (minutes), SE: Sleep Efficiency (%)
In addition to quantifying cross-method concordance, partial correlations were also used to assess whether the behavioural aspects of the CSHQ not measurable by actigraphy (i.e., bedtime resistance, sleep anxiety, daytime sleepiness, parasomnias, daytime sleepiness, sleep disordered breathing) bore any relationship with objective sleep parameters. As shown in Table 4, the parasomnias, sleep anxiety, and SDB subscales were not associated with any objective sleep parameters across both groups, except for a significant relationship between sleep anxiety and sleep offset time/get up time in the TD group. A number of significant relationships were however observed for the bedtime resistance subscale. Specifically, in children with ASD, increased parent-reported bedtime resistance was associated with later bedtime/sleep onset time, shorter total sleep duration, and later time of sleep offset/get up time. Similar associations were seen in the TD group, although bedtime resistance was not associated with later time of sleep offset or decreased total sleep time. Finally, increased daytime sleepiness was significantly associated with later time of sleep offset/get up time across both groups, and with later bedtime in the TD group only.

Discussion

Three core findings emerged from the present study: i) parent-reported sleep disturbance is significantly more prevalent and severe in school-aged children with ASD, compared to age and gender-matched TD children; ii) through the use of objective sleep assessment, difficulties in the initiation of sleep emerged as a prominent feature of the ASD sleep profile, underlying reduced overall sleep efficiency; iii) Parents of children with ASD report longer sleep onset delay, shorter sleep duration and increased night wakings than parents of TD children. When compared to actigraphy, however, only sleep onset latency differentiated between groups and demonstrated a significant association with parent report.
The current study firstly aimed to compare subjective sleep problems and objective sleep patterns in school-aged children with and without ASD. The use of the CSHQ as a standardised screening tool identified 91% of the ASD group and 50% of the TD group were currently experiencing sleep problems; rates similar to other studies utilising the CSHQ in school-aged children (Couturier et al., 2005; Hodge et al., 2014; Souders et al., 2009). Also in line with previous findings from the CSHQ, parents of children with ASD endorsed multiple sleep problems, with the largest effect sizes observed in the sleep duration, night waking and sleep anxiety subscales (Couturier et al., 2005; Hodge et al., 2014; Hoffman et al., 2006; Souders et al., 2009). Additionally, the use of actigraphy to assess sleep patterns has reinforced issues with the initiation of sleep as a core feature of the ASD sleep profile. Of particular note is the increased between and within-child variability in the time taken to initiate sleep in children with ASD compared to TD children. The finding of greater between-child variation in SOL (as evidenced by larger standard deviations between groups) is consistent with previous ASD and TD actigraphy comparisons in school-aged children (Allik et al., 2006; Souders et al., 2009), and likely reflects the heterogeneous nature of the ASD profile. In contrast, the finding of greater within-child variation in SOL (as evidenced through individual participant standard deviations across the fourteen nights) identified greater daily variation in the time taken to initiate sleep in children with ASD compared to TD children, and conflicts with previous findings in pre-school aged children with ASD (Anders, Iosif, Schwichtenberg, Tang, & Goodlin-Jones, 2011). This may reflect a response to the dynamic causes of sleep onset difficulties in school-age children with ASD such as anxiety, diet, and sleep hygiene. Methodologically, the observed within and between-child variations may indicate a need to reassess the way in which sleep in children with ASD is captured and reported.
In accordance with previous findings from a sample of children with ASD without ID, a significantly earlier bedtime was also observed in children with ASD (Allik et al., 2006). Importantly, despite previous suggestions that an earlier bedtime may be responsible for increased SOL (Allik et al., 2006), the initiation of sleep still took significantly longer in our ASD group, after controlling for bedtime. Finally, in line with the previous use of actigraphy in children with ASD without ID, no difference in the maintenance of sleep was found between groups (Allik et al., 2006).

A second key aim of the current study was to examine age-related changes in children’s sleep profiles across the school-aged years. From the CSHQ, older children were characterised by decreased bedtime resistance and sleep anxiety, with interaction effects identified for CSHQ total scores and bedtime resistance. Specifically, group differences were the greatest in the younger (6-8 years) age groups. This supports recent comparisons between children with ASD and TD children, where the difference in CSHQ total scores and bedtime resistance was greatest in the 6-9 age group compared to both younger (3-5 years) and older (10-17 years) individuals; with the authors proposing that increased melatonin dysregulation in younger children may explain the increased susceptibility to sleep problems during this time (Hodge et al., 2014). Furthermore, the examination of age-related changes in actigraphy identified a decrease in total sleep time in older children, compounded by a later bedtime and time of sleep onset. There were no interaction effects for any actigraphy variables, supporting previous longitudinal findings that TD children and children with ASD exhibit a similar developmental trajectory in the timing and duration of sleep (Allik et al., 2008). The absence of a cross-sectional age-related effect in sleep onset latency (SOL) is also consistent with previous longitudinal research, with both ASD age groups taking longer than 30 minutes to initiate sleep (Allik et al., 2008).
Finally, the third aim of the current study was twofold: i) to assess the strength of the relationship between actigraphy variables and comparable CSHQ subscales for three specific aspects of sleep; the time taken to initiation sleep, the ability to maintain sleep throughout the night, and the total amount of time spent asleep each night, and ii) to explore whether behavioural aspects of sleep measured by the CSHQ were associated with any actigraphy-derived sleep variables. Although parents reported significantly greater problems across all three sleep areas (more concerns regarding night wakings, sleep onset, and sleep duration) in children with ASD, only actigraphic SOL (the time taken to initiate sleep) significantly differed between groups. Furthermore, when correlating the CSHQ subscales with actigraphy, only the sleep onset delay subscale displayed the expected associations; with greater parental concerns significantly associated with longer actigraphic SOL, as well as shorter sleep onset and lower overall sleep efficiency. This discrepancy may reflect the notion that sleep onset latency is simply the most observable part of a child’s sleep pattern and given the prominence of sleep onset difficulties in ASD, it is to be expected that parents would be acutely aware of it in their child. In a recent study comparing the CSHQ to actigraphy in TD children and children with clinically diagnosed Generalised Anxiety Disorder (GAD), a similar finding emerged whereby parents of clinically anxious children consistently reported increased sleep problems on the CSHQ, but these were not corroborated by objective sleep assessment. Their conclusions are reiterated here in that ‘sleep problems’ should not be confined to problems that occur during the sleep period and within the bedroom. Numerous other sleep-related issues such as the request to co-sleep, nightmares and bedtime resistance, may not impact upon traditional sleep parameters (e.g., night wakings, total sleep time), but their impact should not be overlooked (Alfano et al., 2015). Indeed, in the current study increased bedtime resistance was associated with delayed sleep onset time and shorter total
sleep time in children with ASD; reinforcing the benefits of utilising actigraphy to complement parent report findings.

The current findings should be interpreted in consideration of the limitations of this study. Firstly, ASD diagnoses were not confirmed by the ‘gold-standard’ diagnostic tools; the ADOS and/or the ADI-R; although it is noted that the current method of diagnostic confirmation (diagnostic report review in conjunction with a screening questionnaire) is an approach used in several previous studies in this area (Allik et al., 2006; Hodge et al., 2014; May et al., 2015). Additionally, a number of children in the ASD group were taking prescription medications, including psychotropic medication for ADHD behavioural symptoms, and medication to aid sleep (i.e., melatonin). However, as discussed in a previous study examining sleep in ASD, the exclusion of medicated children significantly limits the generalisability of the sample (Couturier et al., 2005). For example, previously observed associations between poor sleep quality and higher ratings of inattention and hyperactivity in children with ASD (Goldman et al., 2009; Goldman et al., 2011; May et al., 2015; Mayes & Calhoun, 2009) suggest that the exclusion of such children may lead to selection bias, whereby those children with the most severe sleep problems are excluded. Indeed, research in this age group often chooses not to exclude medicated children (Couturier et al., 2005; May et al., 2015; Schreck & Mulick, 2000; Souders et al., 2009), and instead attempts are made to examine the effect of medication on sleep profiles (May et al., 2015; Souders et al., 2009); as done so in the current study. Finally, it should be highlighted that the use of actigraphy to measure sleep is not without its limitations, particularly around the detection of night wakings (Hodge et al., 2012; Meltzer et al., 2012). However, the collection of fourteen nights of data, the use of the marker button in conjunction with sleep diaries, and manual scoring of gross night wakings serve to maximise the utility of actigraphy in this study (Meltzer et al., 2012). The current research is also strengthened by the exploration of age-
related differences in children’s sleep profiles, the use of a community-recruited ASD sample without ID, and a well-matched TD control group. Furthermore, all TD children were screened for ASD using a validated screening questionnaire, and the FSIQ of all participating children was assessed.

Together these findings validate the increased frequency and severity of sleep disturbance in school-aged children with ASD compared to TD children and highlight the utility of including both parent-report and objective sleep methods. Previous research supports an association between sleep problems and the severity of autistic symptoms and other co-morbid symptoms including anxiety and inattention (Goldman et al., 2011; Hollway, Aman, & Butter, 2013). The current findings, therefore, highlight the need to consider the role of poor sleep in the heterogeneous nature of symptoms in this population of children. Moving forward, given the recent and successful use of ‘home-based’ PSG recording in children with ASD by Maski et al. (2015), further investigation into the utility of such methods should be considered in future paediatric ASD sleep research.
References


Monash University

Declaration for Thesis Chapter 4

Declaration by candidate

In the case of Chapter 4, the nature and extent of my contribution to the work was the following:

<table>
<thead>
<tr>
<th>Nature of contribution</th>
<th>Extent of contribution (%)</th>
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<tbody>
<tr>
<td>Study design, data collection, data analysis, interpretation of results, preparation of manuscript</td>
<td>70</td>
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</table>

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

<table>
<thead>
<tr>
<th>Name</th>
<th>Nature of contribution</th>
<th>Extent of contribution (%) for student co-authors only</th>
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<tr>
<td>Dr K. Johnson</td>
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<tr>
<td>Ms F. Fletcher</td>
<td>Study design, data collection, feedback on prepared manuscript</td>
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<tr>
<td>Dr R. Conduit</td>
<td>Study design, data analysis, interpretation of results, feedback on prepared manuscript</td>
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<tr>
<td>Prof N. Rinehart</td>
<td>Study design, feedback on prepared manuscript</td>
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<tr>
<td>Prof K. Cornish</td>
<td>Study design, interpretation of results, feedback on prepared manuscript</td>
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The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate’s and co-authors’ contributions to this work.

Candidate’s Signature

Main Supervisor’s Signature

Date
07/03/2016

Date
07/03/2016
CHAPTER 4

ATTENTIONAL NETWORK FUNCTIONING IN ASD

Preamble to Paper 2

The aims of this paper are drawn directly from gaps and inconsistencies in the ASD attention literature identified in Chapter 2 (Literature Review). Specifically, the core aim of the current paper was to profile cognitive attention differences between school-age children with Autism Spectrum Disorder (ASD) without intellectual disability (ID), and their typically-developing (TD) peers, using the Attention Network Test for Children (ANT-C) and the several subtests from the Wilding Attention Test for Children. As highlighted in the review, no previous study has utilised the child variant of the ANT to elucidate cognitive attentional differences between these two cohorts. A secondary aim of this paper was to explore age-related differences in children’s attentional profiles; allowing detection of both subtle and overt improvements and deteriorations in children’s cognitive attention profile not previously reported in ASD.


Note: This paper has been submitted to the Journal of Child Neuropsychology

Abstract

Background The Attention Network Test for Children (ANT-C) and Wilding Attention Test for Children (WATT) provide measurement of different aspects of cognitive attention. We ask if children with ASD display a characteristic pattern of attentional difficulties on these tasks. Methods 33 children with ASD without intellectual disability and 60 controls aged 6-12 years completed the ANT-C and subtests from the WATT measuring selective, sustained, and switching attention. Results Younger children with ASD responded more slowly to spatial orienting cues and showed no reaction time differences between cue conditions. Age by group interaction effects were observed for alerting. Children with ASD demonstrated poorer switching and sustained attention. No group differences were seen for orienting and conflict networks, or for selective attention. Conclusions School-age children with ASD exhibit deficit functioning in select aspects of cognitive attention and appear less responsive to visual orienting cues in early childhood.
Autism Spectrum Disorder (ASD) is a complex and pervasive neurodevelopmental condition characterised by impairments in social & communicative functioning, along with stereotyped and repetitive behaviours (American Psychiatric Association, 2013). While these features form the basis for the diagnosis of ASD, abnormalities in attentional functioning are often associated with the disorder. Indeed, rates of comorbid Attention-Deficit/Hyperactivity-Impulsivity Disorder (ADHD) symptoms are reported to range between 22-78% (Lee & Ousley, 2006; van Steensel, Bogels, & de Bruin, 2013), and children with ASD demonstrate elevated rates of behavioural inattention, such as staring into space (Yerys et al., 2009). Researchers have also used sophisticated neuropsychological tasks to assess underlying cognitive aspects of attention, finding deficits associated with ASD (Geurts, Corbett, & Solomon, 2009). These cognitive tasks measure how well information is attended to and processed. Despite a multitude of studies in this area, as a result of the use of different measures across studies and the heterogeneous nature of ASD cohorts, the precise profile of cognitive attention difficulties experienced by children with ASD remains unclear (Geurts et al., 2009). The current study, therefore, sought to elucidate the nature of cognitive attention in a well-defined sample of school-aged children with and without ASD, through the use of two well-validated attention tasks: the Attention Network Test for Children (ANT-C) and the Wilding Attention Test for Children (WATT).

Posner and colleagues developed a widely-accepted and influential theory of attention, which posits that cognitive attention consists of three separate, but interconnected, brain networks coined the ‘alerting’ system, the ‘orienting’ system, and the ‘executive control’ system (Fan, McCandliss, Sommer, Raz, & Posner, 2002; Posner & Petersen, 1990; Posner & Rothbart, 2007). The alerting network facilitates the ability to attain and sustain a high state of alertness to incoming stimuli (Cornish & Wilding, 2010). The orienting network disengages and shifts attention from one point to another (Renner, Klinger, & Klinger, 2006).
Finally, executive control regulates attentional processes such as planning, maintenance of conflicting information, and inhibition (Posner & Petersen, 1990; Raz, 2004; Rothbart, Sheese, & Posner, 2007). Conceptualisation of attention in this way has facilitated exploration of individual differences in network efficiency, particularly in populations known to experience attentional difficulties (e.g. ADHD, brain injury), and the subsequent development of an experimental computerised task to measure the efficiency of these three networks simultaneously: The Attention Network Test (Fan et al., 2002).

These attention networks are active in early childhood and continue to develop into adulthood. In typically-developing (TD) children each network appears to have a different developmental trajectory (Pozuelos, Paz-Alonso, Castillo, Fuentes, & Rueda, 2014; Rueda et al., 2004), although research findings are inconsistent. In terms of alerting, Rueda et al. (2004) reported no significant change between the ages of 6 to 10 years, but significantly faster RTs in adults (aged 19-41 years) compared to 10-year-old children. More recently, improvements have been reported between the ages of 6-12 years, with significantly faster RTs observed in children aged 8-12 years compared to children aged 6-7 years, and progressive improvement seen from age 8 to 12 years (Pozuelos et al., 2014). Inconsistent findings are also reported for orienting. Whilst Rueda et al. (2004) reported no significant differences in orienting RT scores between the ages of 6 and 10 years, or between 10 year-olds and adults, Pozuelos and colleagues (2014) found significantly larger RT scores between 6-year-olds and children aged 7, 10, and 12 years, respectively. In terms of executive control, Rueda et al. (2004) reported significant improvements in RT from the age of 6 to 7 years, but no significant differences between the ages of 7 to 10 years, or between 10 year-olds and adults. In contrast, planned comparisons in children aged 6-12 years found significant reductions in RTs between the ages of 6-8 and 9-12 years (Pozuelos et al., 2014). Taken together, these findings indicate ongoing development in attentional networks across middle
childhood and into adulthood and highlight the need for further research into the development of these networks in TD children.

Only one previous study has used the ANT to examine attention control in children with ASD (Keehn, Lincoln, Muller, & Townsend, 2010). Utilising the adult ANT, Keehn and colleagues (2010) found significant group differences in the orienting network only, with children aged 8-19 years with ASD demonstrating less efficient orienting. In addition, greater interdependence was measured between the alerting and executive control networks in the ASD group, but not in the control group (Keehn et al., 2010). One methodological problem with this study was that the incongruent flanker trials were included in the calculation of the alerting and orienting networks, thus confounding interference control with attention control. A clearer understanding of the functioning of the alerting and orienting networks in ASD is therefore needed.

A child-friendly version of the task has been adapted in order to study the development of these attention networks in children (Rueda et al., 2004). In this version, children are presented with colourful yellow fish, displayed on a blue background, in place of the black static arrows in the adult version. Children are also provided with (a) a story that encourages them to “feed the hungry fish” and (b) feedback on their performance after each trial. These additions are based on research finding that children respond best, and are more engaged on tasks when provided with clear feedback and a story (Berger, Jones, Rothbart, & Posner, 2000). To date, no study has utilised the child-friendly version of the ANT, or examined age-related changes on ANT performance, in children with ASD.

Psychometric evaluation of the adult version of the ANT reported low split-half reliability for the alerting and orienting networks and has suggested using additional tasks, measuring refined components of attention, for converging evidence on the functioning of specific attention networks (Macleod et al., 2010). One battery designed to elucidate select
components of attention is the WATT (Wilding, Munir, & Cornish, 2001). The WATT is comprised of computerised visual search tasks measuring selective attention, sustained attention, and aspects of executive control separately. To date, only one previous study has utilised subtests from the WATT to study sustained and switching attention in ASD. 60 children with ASD aged 7-12 years without intellectual disability (ID), and their age-and-gender-matched TD peers were tested twice, one year apart (May, Rinehart, Wilding, & Cornish, 2015). Whilst no significant difference was found between the groups for sustained attention, the ASD group made significantly more errors during attention switching, at both time points (May et al., 2015), suggesting deficient functioning in the orienting network in ASD.

In the current study, our goal was to investigate the utility of the ANT-C, alongside the WATT, as measures of attention in school-age children with ASD without ID and explore age-related differences on task performances. The first aim was to compare children’s performances on both the ANT-C and WATT. It was hypothesised that children with ASD would demonstrate deficient functioning in the orienting network on both tasks. The second aim was to explore the effect of age on attention performance. It was hypothesised that older children, compared with younger children, would demonstrate superior attention control on both the ANT-C and WATT. Finally, we aimed to investigate whether the ANT-C or the WATT or specific aspects of each task/battery, were better at differentiating children with ASD from TD children. It was hypothesised that both the orienting network score from the ANT-C and the switching task from the WATT would differentiate those children with ASD from TD children.

**Method**
Participants

A total of 93 community-recruited children participated in this study. Criteria for inclusion were: aged between 6;0 and 12;11 years; English as a first language; and Full-Scale IQ (FSIQ) above 70. Children were excluded from participation if they had any history of seizure disorder or any medical conditions that significantly impacted hearing, vision, or motor control.

ASD Group. 33 children with ASD (22 males, age range 6;0-12;10 years) were recruited through several ASD services including; AMAZE, Asperger Syndrome Support Network Victoria, Melbourne Children’s Clinic, speech therapists, and parent support groups. Comprehensive and multidisciplinary diagnoses of Autistic Disorder, Asperger’s Syndrome, or ASD were completed by a paediatrician or registered psychologist, independent from the current research project, prior to children’s participation in the current study. Diagnostic reports were obtained from parents and checked against the DSM-IV-TR symptom checklist to ensure criteria were met. Children were additionally screened using the Social Responsiveness Scale (SRS; Constantino & Gruber, 2002).

TD Group. 60 TD children (33 males, age range 6;1-12;6 years) were drawn from a larger sample of 95 children who participated in Monash University’s ‘Networks of Attention and Paediatric Sleep’ (NAPS) project, recruited via primary schools, print media, community centres, and webpage advertisements. Children were excluded if they had a diagnosis of any neuropsychiatric disorder, obtained an SRS T-score $\geq$75, had a sibling with ASD, or were without ANT-C data.

Measures

Demographics and Medical History: Demographic information and medical history were obtained from parents using a semi-structured interview. Socio-economic information
was obtained using a brief questionnaire. A socioeconomic status score indicating relative socioeconomic advantage/disadvantage was calculated using the Socio-economic Indexes for Areas data from the Australian Bureau of Statistics (ABS SIEFA; 2013), based on participants’ residential postcodes. All areas were allocated a decile number ranging from 1 to 10 where 1 indicated the most disadvantaged area and 10 indicated the most advantaged area.

**Intellectual Functioning:** The two-subtest (vocabulary and matrix reasoning) version of the *Wechsler Abbreviated Scale of Intelligence* (WASI; Wechsler, 1991) was completed for all children. The WASI is a short and reliable measure of intelligence, suitable for use with individuals aged 6-89 years. It yields an FSIQ comparable to the Wechsler Intelligence Scale for Children – Third Edition (WISC-III; Wechsler, 1991) FSIQ. Intercorrelations between FSIQ scores derived from the two and four subtest versions of the WASI range from .91 to .97 (Wechsler, 1999).

**Autistic Symptoms:** The *Social Responsiveness Scale* is a 65-item parent-completed questionnaire, designed to measure autistic traits in children aged 4-18 years (Constantino & Gruber, 2005). Items are rated on a four-point Likert scale where 1 is “not true” and 4 is “almost always true,” based on behaviour during the previous six months. The questionnaire yields a total score, which can be converted to a T-score, and provides an indicator of the severity of social impairment. T-scores ≥75 have been found to discriminate children with and without ASD with specificity and sensitivity values of .75 and .85, respectively (Constantino et al., 2003). Correlations between SRS scores and Autism Diagnostic Interview-Revised domain scores range from .65 to .77 (Constantino et al., 2003).

**Behavioural Attention:** The *Conners’ Parent Rating Scale – 3rd Edition – Long Form* (CPRS-3-LF; Conners, 2008) is a caregiver-completed, 108-item questionnaire designed to measure behaviours relating to ADHD (i.e. inattention, hyperactivity etc.), and the most
commonly associated co-morbid disorders and problems in children aged 6-18 years (Gallant et al., 2007) Items are rated on a four-point Likert scale where 0 is “not true at all” and 3 is “very much true” based on the child’s behaviour during the past month. Internal consistency ranges from 0.83 to 0.94 (Gallant et al., 2007).

**Cognitive Attention:** Computerised attention tasks were presented on an HP laptop running Windows XP, with a 19-inch screen. The *Attention Network Test -Children* (Rueda et al., 2004) was programmed to run on E-Prime, and responses made on the laptop mouse-pad. Each trial commenced with a centrally located fixation cross (see Figure 1). The random variable duration of the fixation period was between 400 and 1600ms. Presentation of each target stimulus was preceded by one of four cue conditions: no cue, central cue, double cue, and spatial cue. In the no cue condition, the target was not preceded by any cue. In the central cue condition an asterisk was presented at the same location as the central fixation cross. In the double cue condition two asterisks were presented; one above the fixation cross and one below the fixation cross. In the spatial cue condition, a single asterisk was presented at the location of the upcoming target, either above or below the fixation cross. All cues were presented for a period of 150ms. Following the disappearance of each cue type participants were presented with a fixation period of 450ms before the appearance of the target stimuli. Target stimuli consisted of either a single fish (neutral condition), a horizontal array of five fish facing the same way (congruent condition), or a central fish flanked on each side by two fish facing the opposite direction (incongruent condition), either below, above, or at the central fixation point. Targets were single fish in the neutral condition and central fish for congruent and incongruent conditions. Children were instructed to press the left button if the target fish was facing left and the right button if it was facing right, in order to “feed the hungry fish.” Children were allowed 1700ms to respond to each trial, after which the trial was recorded as missed. After a response was made or a trial timed out children received
either positive auditory (“Woohoo”) and visual (bubbles from target fish’ mouth) feedback for correct responses, or negative auditory (negative tone) feedback for incorrect (response made in opposite direction to target fish) or missed trials (omission errors). Each session of the ANT-C took approximately 20 minutes to administer and consisted of 24 practice trials, and 144 test trials divided into three test blocks of 48 trials. Each test block consisted of four randomly distributed trials of each of the 12 conditions (3 flanker conditions x 4 cue conditions).
**Figure 1.** Illustration of The Attention Network Test for Children (ANT-C) experimental procedure including fixation point, cues types, flanker types (targets), and visual feedback.
Children also completed three visual search conditions from the *Wilding Attention Test for Children* (Wilding et al., 2001). Each condition consisted of a screen display of various shapes (“holes”) of differing colours and sizes, on a green background, designed to measure aspects of cognitive attention in children aged 4-16 years. The first condition, *Visearch*, was a single-target conjunctive visual-search task measuring selective attention. Stimuli consisted of 25 target shapes (black vertical ellipses) and 74 distracters (black horizontal ellipses, black circles, brown horizontal and vertical ellipses, brown circles, and large green ellipses containing small brown rectangles) presented simultaneously. Children were instructed to click on “black ovals standing up” as fast as possible until they had found the “king monster.” The first 19 targets revealed small blue monsters. The king monster always appeared at the 20th target. If the participant was unable to find the king after 50 responses the condition terminated. The second condition, *Visearch-Dual*, was a dual-target visual-search task assessing attentional switching. Stimuli consisted of 30 targets (15 black vertical ellipses and 15 brown horizontal ellipses) and 70 distracters (black horizontal ellipses, black circles, brown vertical ellipses, brown circles, and large green ellipses containing small brown rectangles), presented simultaneously. Children were instructed to switch between clicking on “black ovals standing up” and “brown ovals on their side”, and to continue switching between the two, as fast as possible, until they found the “king monster”. Black vertical ellipse targets revealed small blue monsters and brown horizontal ellipse targets revealed small yellow monsters. The king monster always appeared at the 20th target. If the participant was unable to find the king after 50 responses the condition terminated. The third condition, *Vigilan*, assessed vigilance/sustained attention. Children were instructed to search the “whole forest” (screen) and click on “holes” as quickly as possible if a yellow ring appeared around them, as this indicated a monster was hiding there until they found the king. The yellow ring appeared around black vertical ellipses at irregular intervals of between 4-14
seconds. Rings would remain around targets for 7 seconds before disappearing. If children clicked on targets within 7 seconds a small monster would appear. The king monster always appeared at the 15th target. If the participant was unable to locate and click on 15 targets within 4 minutes the condition terminated.

**Procedure**

Upon contact by the parent/guardian, screening was conducted to ascertain whether the child met eligibility criteria. Eligible children were tested on two separate occasions, 14-15 days apart, either within their home or the research laboratory. The first session involved obtaining informed written consent, distribution of parent questionnaires, and administration of the WASI. At the second session, children completed a 40-minute attention test battery. For both sessions, children were seen individually in a quiet room during cognitive testing. All children completed the ANT-C first, followed by the WATT attention battery in the following order: Visearch, Visearch-dual, and Vigilan. Children completed a practice trail for the Visearch & Vigilan conditions but not for Visearch-dual.

**Data Analyses**

All analyses were performed using SPSS, version 22 for Windows (IBM Corp, 2013). The data set was assessed for univariate outliers within groups using z-scores. Any z-scores greater than ±3.29 were transformed to one value higher than the next highest/lowest non-outlier in order to reduce their influence. Type 1 error was controlled in post-hoc comparisons through Bonferroni adjustment. Comparisons between the ASD and TD groups for categorical and continuous variables were accomplished using χ² analysis, Mann-Whitney U, and T-tests. Six TD children were without behavioural attention data as parents did not complete the Conners. Mann-Whitney U tests were utilised for the Conners inattention and
hyperactivity/impulsivity subtests as they were non-normal in distribution. Prior to the examination of cognitive attention variables, each diagnostic group (ASD vs. TD) was divided into Younger [aged 6;0 to 8;11 years, ASD M (SD) = 88.16 (10.50) and TD M (SD) = 90.17 (9.54) months] and Older [aged 9;0 to 12;11 years, ASD M (SD) = 130.93 (16.27) and TD M (SD) = 127.64 (14.46) months] age groups, to allow exploration of age-related differences.

ANT-C data from two children in the ASD group were excluded; one due to sensitivity to the auditory feedback that invalidated task performance (female), and the other due to an omission rate >50% (male). In line with Johnson et al. (2008), the Alerting index was calculated by subtracting mean RT in the double cue condition from the no cue condition, collapsed across neutral and congruent flanker conditions, and the Orienting index was calculated by subtracting average RT in the spatial cue condition from the centre cue condition, collapsed across neutral and congruent flanker conditions. In line with Fan et al. (2002), calculation of the Executive Control index was accomplished by subtracting mean RT in the congruent flanker condition from the incongruent condition, collapsed across all cue conditions. Higher alerting and orienting RT index scores indicate less benefit from alerting and orienting cues, respectively (e.g. poor use of cues). Higher Executive Control index scores indicate more difficulty resolving conflicting information (e.g. more interference from incongruent flankers). Main ANT-C RT comparisons were accomplished using three-way, and four-way mixed-model ANOVAs. The Greenhouse-Geisser estimate of the F statistic was used when Mauchley’s test of sphericity was significant. Univariate two-way ANOVA’s with both Group and Age included as between-subject factors were used to examine Mean RT differences for each calculated attention network score, and an alpha level of .01 applied where Levene’s test of Equality of Error Variance was violated. Nonparametric Mann-
Whitney U and Friedman tests were utilised for OEs and IRs as they were non-normal in distribution.

Data for three children in the TD group and one child in the ASD group, across all three WATT subtests, was lost due to technological issues. Additionally, one child in the TD group and one child in the ASD group were missing data for the Vigilan task only. Mean ‘false alarms’ for each subtest of the WATT were analysed in univariate two-way ANOVA’s with both Group and Age included as between-subject factors. Mean ‘hits’ were analysed for sustained and switching attention only as both groups performed at ceiling (20 hits) for the selective subtest. An alpha level of .01 was applied where Levene’s test of Equality of Error Variance was violated. The Greenhouse-Geisser estimate of the F statistic was used when Mauchley’s test of sphericity was significant.

Results

Sample characteristics

Sample characteristics are reported in Table 1. The groups did not differ significantly in terms of gender, χ²(1, N = 93) = 1.20, p = .27, age, t (91) = 0.10, p = .99, or SES, t (91) = 0.60, p = .55. The TD group had a significantly higher average FSIQ than the ASD group, t (91) = 5.04, p < .001. The ethnicity of each group was primarily Caucasian, and an undergraduate degree was the most frequent level of primary-caregiver education. As expected, SRS total scores were significantly greater for the ASD group, t (42.03) = 15.37, p < .001. The ASD group was also rated significantly higher on the Inattention [U =139.50, p < .001] and Hyperactivity/Impulsivity subscales [U =156.50, p <.001] compared with the TD group.

Examination of within-group differences on behavioural attention measures revealed similar ratings of Inattention [U =110.00, p = .40] and Hyperactivity/Impulsivity [U =125.50,
between the younger and older ASD age groups. The TD group showed no significant difference between age groups for Inattention \([U = 350.50, p = .92]\), but a significant reduction in parent-reported Hyperactivity/Impulsivity in the Older age group \([U = 226.00, p = .022]\).

Table 1. Participant characteristics for the ASD and TD groups

<table>
<thead>
<tr>
<th></th>
<th>ASD ((n=33))</th>
<th>TD ((n=60))</th>
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<tbody>
<tr>
<td><strong>Gender (males) n (%)</strong></td>
<td>22 (66.7)</td>
<td>33 (55.0)</td>
</tr>
<tr>
<td><strong>Age (months) M (SD)</strong></td>
<td>106.30 (25.11)</td>
<td>105.78 (22.01)</td>
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<td><strong>FSIQ M (SD)</strong></td>
<td>98.82 (14.11)***</td>
<td>114.22 (14.09)***</td>
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<tr>
<td><strong>Ethnicity n (%)</strong></td>
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<td>Caucasian</td>
<td>31 (93.9)</td>
<td>54 (90.0)</td>
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<tr>
<td>Other</td>
<td>2 (6.1)</td>
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<tr>
<td><strong>Primary Caregiver Education n (%)</strong></td>
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<td>Partial High school</td>
<td>3 (9.1)</td>
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</tr>
<tr>
<td>Completed High School</td>
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<tr>
<td>Some University</td>
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<td>Undergraduate Degree</td>
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<td>3 (5.0)</td>
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<tr>
<td><strong>SES Score M (SD)</strong></td>
<td>7.79 (2.04)</td>
<td>7.48 (2.48)</td>
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<tr>
<td><strong>SRS Total M (SD)</strong></td>
<td>96.94 (25.67)***</td>
<td>23.17 (13.55)***</td>
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<tr>
<td><strong>Conners 3 Subscales M (SD)</strong></td>
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<tr>
<td>Inattention</td>
<td>19.39 (6.64)***</td>
<td>6.44 (5.11)***</td>
</tr>
<tr>
<td>Hyperactivity/Impulsivity</td>
<td>26.30 (9.13)***</td>
<td>6.85 (7.05)***</td>
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</table>

### Notes

***≤.001

TD: Typically-developing, ASD: Autism Spectrum Disorder, FSIQ: Full-scale IQ,

SES: Socioeconomic Status, SRS: Social Responsiveness Scale

Seventeen participants with ASD (51.5%) were taking prescription medication at the time of testing, and six of these children were taking more than one medication. The most commonly prescribed medications were melatonin (21.2%) and SSRI’s (12.1%). Three
children (9.1%) were taking stimulant medication (Ritalin, $n=1$; Concerta, $n=1$; dexamphetamine, $n=1$), three were taking an atypical neuroleptic (9.1%), and one child was taking Atomoxetine (a norepinephrine reuptake inhibitor used to treat ADHD symptoms). Additionally, two children (6.1%) were taking anticonvulsant medication prescribed as a mood stabiliser and three children (9.1%) were taking clonidine.

**ANT-C Response Time Analysis**

Mean RT was analysed in a Group (ASD vs. TD) by Age (younger vs. older) by Flanker (congruent, neutral, incongruent) by Cue (no, centre, double, spatial) four-way mixed-model ANOVA design. A significant Group by Age by Cue interaction was seen, $F(3, 87) = 5.97, p = .001$, partial $\eta^2 = .064$. Follow-up two-way (Group x Cue) mixed-model ANOVAs for each age group (older and younger) showed a significant interaction between Group and Cue for the younger (6 to 8 years) age group only, $F(3, 50) = 5.28, p = .002$, partial $\eta^2 = .095$. Younger TD children responded significantly quicker to the targets when provided with a Cue [centre ($M = 868.76$, $SD = 133.30$), double ($M = 842.18$, $SD = 145.55$), spatial cue ($M = 819.78$, $SD = 142.20$)], compared with the no cue condition ($M = 940.37$, $SD = 131.98$), all $p$s < .001. They were also faster to respond to targets after the spatial compared with the centre cue, $p < .001$. In contrast, younger children in the ASD group responded significantly quicker to the targets when provided with the double cue ($M = 925.93$, $SD = 145.55$) compared with the no cue condition ($M = 975.65$, $SD = 131.98$), $p = .040$, but demonstrated no significant difference in Mean RTs between the no, centre ($M = 936.00$, $SD = 133.30$), or spatial cue ($M = 931.87$, $SD = 142.20$) conditions (see Figure 2). In addition, pairwise comparisons demonstrated that Younger TD children responded significantly faster to targets when presented with a spatial orienting cue than the Younger ASD group, $p = .010$. 
No other differences were observed between the younger ASD and TD groups on any other cue types.

Figure 2. Mean RT’s (ms) for ASD and TD Younger and Older children in response to each cue type on the Attention Network Test for Children (ANT-C).

A significant main effect for Flanker was obtained, $F(1, 89) = 82.23, p < .001$, partial $\eta^2 = .49$, with pairwise comparisons showing that Mean RT was significantly faster in the neutral condition ($M = 770.01, SD = 138.17$) versus both the incongruent ($M = 853.68, SD = 157.71, p < .001$) and congruent ($M = 788.57, SD = 141.45, p = .002$) conditions, and significantly faster in the congruent versus the incongruent condition, $p < .001$. There were no significant interactions between Flanker and Group, Flanker and Cue, or Flanker and Age (all $ps > .05$).

ANT-C Attention Network Scores

Calculated attention network scores were analysed separately in Group (ASD vs. TD) by Age (Younger vs. Older) two-way ANOVA’s (see Table 2). Where Levene’s test of Equality of Error Variance was violated an alpha level of .01 was applied to assess significance. No significant Group or Age main effects were identified in mean RT for the Alerting, Orienting,
or Executive attention networks. A significant interaction between Group and Age was seen, however, for the Alerting network score, $F(3, 87) = 5.75, p = .019$. Examination of means indicated that the Older TD group showed a larger difference in mean RT between the double and no cue conditions (i.e., a higher ‘alerting score’) compared to the younger TD group; likely indicating good use of cues. The ASD group demonstrated the opposite effect with the older age group found to benefit less from the provision of a warning cue versus no cue (i.e., a lower ‘alerting score’) than younger children with ASD (see Figure 3). Despite this significant interaction, pairwise comparisons did not reach significance which may reflect the large amount of within-group variation.
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* $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$, *Indicates Levene’s test was violated

TD: Typically-developing, ASD: Autism Spectrum Disorder
**ANT-C Error Analysis**

*Omission errors*

No significant difference was observed between groups for total number of OEs (ASD: $M = 8.81$, $SD = 12.15$, TD: $M = 5.05$, $SD = 5.55$ [$U = 812.50$, $p = .32$]). However, both groups made significantly fewer OEs with older age (ASD: [$U = 53.50$, $p = .008$], TD: [$U = 284.00$, $p = .020$]). Given the significant Group by Age by Cue interaction for Mean RT, focused group comparisons within the younger age group only (i.e., 6-8yrs ASD group vs. 6-8yrs TD group) were conducted for each Cue type (No, Center, Double, Spatial) using the Mann-Whitney Test. No significant differences were seen between groups for number of OEs for any of the Cue conditions (all $ps > .05$).

Within-group differences for OEs, between the four cue conditions, were analysed for each age and diagnostic group separately using Friedman’s ANOVA. The younger children in the ASD group made a similar number of OEs [$\chi^2 (3) = 2.80$, $p = .42$] over the four cue types; in contrast the younger children in the TD group demonstrated a significant difference in the number of OEs made [$\chi^2 (3) = 14.11$, $p = .003$]. This was followed up with Wilcoxon’s signed-rank test with the Bonferroni adjustment for Type 1 error ($\alpha = .008$). Wilcoxon signed rank tests indicated a significant decrease in OEs in both the Double and Spatial cue conditions compared to the No Cue condition ($T = 41.50$, $z = -3.45$, $N – Ties = 26$, $p = .001$, $r = .13$ and $T = 25.00$, $z = -2.87$, $N – Ties = 19$, $p = .004$, $r = .15$ respectively). Older children in the TD group made a similar number of OEs across the four cue types, [$\chi^2 (3) = 7.65$, $p = .054$]. Whilst Friedman’s ANOVA indicated that Older children in the ASD group showed a significant difference in the number of OEs made across the four cue types, [$\chi^2 (3) = 8.26$, $p = .041$], subsequent analysis using Wilcoxon signed rank tests found no significant difference in the number of OEs made between each cue condition at our adjusted alpha level (all $ps > .008$).
Incorrect responses

No significant Group difference was observed for total IRs, (ASD: $M = 6.84, SD = 8.94$, TD: $M = 3.62, SD = 4.04$ [$U = 774.50$, $p = .19$]). Similarly, total number of IRs across all conditions did not significantly differ between age groups in either the ASD [$U = 85.50$, $p = .18$] or the TD [$U = 342.00$, $p = .15$] group. Given the significant Group by Age by Cue interaction for Mean RT, focused between-group comparisons within the younger age group only (i.e., 6-8yrs ASD group versus 6-8 TD group) were conducted for each Cue type (No, Center, Double, Spatial) using the Mann-Whitney Test. No significant differences were seen between groups for number of IRs for any of the Cue conditions (all $ps > .05$).

Within-group differences for IRs, between the four cue conditions, were analysed for each age and diagnostic group separately using Friedman’s ANOVA. The younger children in both the ASD and TD groups made a similar number of IRs over the four cue types, $\chi^2 (3) = 2.91, p = .41$, $\chi^2 (3) = 1.40, p = .71$, respectively. Similarly, older children in the ASD and TD groups did not display any significant difference in IRs across the four cue conditions, $\chi^2 (3) = 3.99, p = .26$, $\chi^2 (3) = 2.23, p = .53$, respectively.

WATT Main Analysis

Mean ‘false alarms’ for each subtest of the WATT, and mean ‘hits’ for the sustained and switching attention tasks, were analysed in Group (ASD vs. TD) by Age (Younger vs. Older) two-way ANOVAs, and results presented in Table 2. Where Levene’s test of Equality of Error Variance was violated an alpha level of .01 was applied to assess significance.

Whilst no significant main effect of group was seen for mean ‘false alarms’ for the selective task, a significant main effect for age was evident, $F (3, 85) = 11.30, p = .001$; with a reduction in errors observed in older children on this task. The interaction between age and group did not reach significance at the adjusted alpha level $F (3, 85) = 4.54, p = .036$. 

Significant Group and Age main effects for mean ‘false alarms’ on the switching attention task were further explained by a significant Group by Age interaction $F(3, 85) = 12.99, p = .001$ (see Figure 3). Whilst number of ‘false alarms’ for the switching attention task was similar between younger and older TD children, $t(55) = .92, p = .36$, a significant reduction was seen in the number of ‘false alarms’ made by older versus younger children in the ASD group, $t(30) = -3.18, p = .003$. A significant group effect was also seen for mean total ‘hits’, with children in the ASD group making significantly fewer hits overall $F(3, 85) = 7.81, p = .006$. Main age and interaction effects for total ‘hits’ did not reach significance at the adjusted alpha level, $F(3, 85) = 4.56, p = .036$ and $F(3, 85) = 5.42, p = .022$, respectively.

**Figure 3** Significant interaction effect between age and diagnostic group for the Switching attention subtest.

Significant main effects of group were seen for the sustained attention task, whereby the ASD group made significantly more errors, $F(3, 83) = 14.19, p < .001$, and significantly less ‘hits’ than the TD group, $F(3, 83) = 6.97, p = .010$. No significant age effects were seen for mean ‘false alarms’ for the sustained attention task, $F(3, 83) = .38, p = .54$. A significant
age effect was seen for mean total ‘hits’, $F(3, 83) = 37.96, p < .001$, with an increase in ‘hits’ observed in older children on this task. An interaction between age and group did not reach significance at the adjusted alpha level for mean ‘false alarms’, $F(3, 83) = 5.73, p = .019$, or mean total ‘hits’, $F(3, 83) = 1.04, p = .31$.

**Comparing the ANT-C and WATT Subtests**

Logistic regression was employed within each age group (Younger and Older) separately in order to assess which aspects of cognitive attention were best able to predict a diagnosis of ASD. Preliminary analyses were conducted to ensure no violation of the assumption of multicollinearity. The three ANT-C network scores (alerting, orienting, conflict) and the false alarms scores for each of the WATT attention tasks (selective, switching, and sustained) were entered into the model together. For the younger age group (6 to 8 years), the full model containing all predictor variables was statistically significant, $\chi^2(6, N = 47) = 25.42, p < .001$, indicating that the model was able to distinguish between children with and without a diagnosis of ASD. The model as a whole explained between 41.8% (Cox and Snall R square) and 58.5% (Nagelkerke R squared) of the variance in group membership, and correctly classified 85.1% of cases. Hosmer and Lemeshew test results confirmed that the model was a good fit for the data $\chi^2(7, N = 47) = 3.58, p > .05$. Analysis of predictor variables showed that after accounting for all other variables, only Switching Attention (number of false alarms) made a unique statistically significant contribution to the model, recording odds ratio of 1.2; indicating that children with ASD aged 6 to 8 years were approximately 1.2 times more likely to display difficulty with switching attention (see Table 3).

**Table 3. Predictor Coefficients for Models Predicting ASD Diagnosis**
For the older age group (9 to 12 years) the full model containing all predictor
variables was statistically significant, $\chi^2 (6, N = 38) = 21.073, p = .002$, indicating that the
model was able to distinguish between children with and without a diagnosis of ASD. The
model as a whole explained between 42.6% (Cox and Snall R square) and 58.2% (Nagelkerke
R squared) of the variance in group membership. The model was 81.6% accurate in its
prediction of diagnostic group. Hosmer and Lemeshew test results confirmed that the model
was a good fit for the data $\chi^2 (8, N = 38) = 5.75, p > .05$. Analysis of predictor variables
showed that after accounting for all other variables, number of false alarms on the sustained
attention task was the only predictor that significantly improved the model’s predictive
capability, recording an odds ratio of 1.42. This indicated that children with ASD aged 8 to
12 years were approximately 1.4 times more likely to display difficulty with sustaining their
attention (as evidenced by greater false alarms) than TD children aged 8 to 12 years (see
Table 3).

**Discussion**

The aim of the current study was threefold; 1) to investigate whether school-aged
children with ASD, without ID, exhibited unique profiles of cognitive attention on the ANT-
C and WATT compared to their age and gender-matched TD peers; 2) to investigate whether children with ASD exhibited similar development of attention, and attentional networks, over middle childhood; and 3) to explore which task, and/or aspect/s of each task, best-delineated children with ASD from their TD peers. Analysis of children’s performances across both tasks revealed that children with ASD not only exhibited deficit functioning in select aspects of cognitive attention but also appear less responsive to visual orienting cues in early childhood, compared to TD children. Analysis of both tasks indicated that the false alarm measure from the switching and sustained attention subtests from the WATT appeared more sensitive, and were better able to distinguish children with ASD from their TD peers, than the ANT-C.

Ineffective Use of Cues

Younger children (aged 6 to 8 years) with ASD appeared to experience difficulties utilising the cues to improve performance compared with their TD peers. This was evidenced by the lack of demonstrated benefit in response time from the provision of the Spatial cues over the No Cues and Centre cues. Whilst slower, younger ASD children were as accurate as TD children under these cue conditions. These findings suggest that younger children with ASD may be less receptive to the information provided in the cues. The exception is their speeded response to the target following the very alerting double cue. This response to the double cue is reminiscent of the reduction in omission errors in trials following the double cue by children with ADHD (Johnson et al., 2008). The lack of receptivity to the informative cues was not evident in the older ASD group (aged 9 to 12 years), indicating that effective use of these cues may simply be delayed in children with ASD.
ANT-C Attention Networks

A significant group by age interaction was observed for the Alerting network; whereby TD children showed improved use of alerting cues with older age whilst the ASD group showed the inverse relationship. This developmental difference in Alerting efficiency was evident in terms of slowed RTs only, with no between or within-group age-related differences observed in terms of task accuracy. Together these findings indicate that while TD children demonstrate improvements in tonic alertness in later childhood, children with ASD do not exhibit similar improvements with older age but show intact ability to utilise external cues to improve task performance. Tonic alertness is believed to be driven by norepinephrine; synthesised in the locus coeruleus, and endogenously controlled and maintained by right lateralised frontal and parietal networks; including the right prefrontal cortex (Posner & Petersen, 1990; Posner, Sheese, Odludas, & Tang, 2006). Imaging studies have demonstrated frontal lobe hyperplasia in children with ASD across the pre-school years (Carper, Moses, Tigue, & Courchesne, 2002; Courchesne, Campbell, & Solso, 2011; Courchesne et al., 2001), followed by a period of abnormally slow growth in these areas in middle to late childhood (Courchesne et al., 2011; Kosaka et al., 2010). In addition recent research has demonstrated reduced activation in inferior and medial prefrontal cortical areas, (alongside striato-thalamic and cerebellar areas), compared to TD children, during a sustained attention/vigilance task; and, in contrast to TD children, no association found between increasing age and activation of these areas (Murphy et al., 2014). Together these findings suggest that abnormal development of the frontal lobes may play some part in the atypical development of the Alerting network via frontal-parietal pathways. Keehn et al (2010), hypothesised that their finding of equivocal alerting between TD children and older children and adolescents with ASD may reflect “a compensatory executive processing mechanism” in
ASD; with a significant association found between the alerting and executive control score in their study. The current study ensured calculation of the alerting network without influence from these conflict processes, however, there is some concern that the exogenously arousing feedback mechanisms built into the ANT-C, but not the adult ANT, may be impacting accurate measurement of this network.

In contrast to previous research examining attentional network functioning in children and adolescents aged 8-18 years with ASD (Keehn et al., 2010), children aged 6-12 years with ASD did not demonstrate reduced efficiency of the Orienting network. While it is possible that this previously observed inefficiency in orienting may simply not become pronounced until later childhood in children with ASD, and thus not evident in our younger sample of 6-12-year-olds, our finding of a lack of demonstrated benefit from the provision of spatial orienting cues in younger children with ASD only, does not support this hypothesis. This finding parallels research conducted in children with ADHD in which no significant effect was seen in terms of the orienting network on the ANT (Booth, Carlson, & Tucker, 2007; Johnson et al., 2008), but significant differences observed between ADHD and TD groups on other tasks measuring attention orienting (Brandeis et al., 2002; Swanson et al., 1991). This suggests that the ANT and ANT-C may not be a sensitive measure of the orienting network in these populations. Alternatively, the large amount of variance observed across all three calculated attention networks scores from the ANT-C within the current sample may be masking true differences between groups.

Children with ASD also did not differ from TD children across either age group in the efficiency of the Executive Control network on the ANT-C. This finding is consistent with Keehn et al. (2010) in an older sample of children with ASD and supports intact efficiency of the executive control network in children with ASD and/or effective utilisation of underlying compensatory mechanisms.
WATT Performance

Switching Attention

As hypothesised, significantly more false alarms were seen in the ASD group overall, with improvements in task accuracy, across both groups, observed with older age. A significant interaction revealed that younger children with ASD made more errors than younger TD children, whilst error rates between older TD and ASD children were similar. Similarly, longitudinal research by May et al. (2015) found that children with ASD demonstrated a significant reduction in the number of false alarms over a year, whilst making significantly more errors than TD children at both time-points.

Sustained Attention/Vigilance

Consistent with May et al. (2015), the current study found significant differences between ASD and TD groups on task accuracy (i.e., false alarms) and target detection (i.e., total hits) on a test of sustained attention. Furthermore, both groups in the current study showed significant improvements in the number of targets found with increasing age, but not in the number of false alarms made; with the Older ASD group making more false alarms than the Younger ASD group (although this difference did not reach statistical significance). This finding of decreased task accuracy in older children with ASD may relate to the previously observed differences between older TD and ASD children in alerting; with sustained attention/vigilance closely tied to this attention system (Hurst, 2013). Alternatively, it may reflect the employment of a strategy that emphasises target detection at the expense of task accuracy by older ASD individuals. This finding further implicates the involvement of the frontal lobes in atypical ASD attentional processing.
Selective Attention

Whilst no overall group difference was seen for selective attention, both groups demonstrated age-related improvements; with enhanced selective attention (i.e., fewer false alarms) observed in older children. This finding is consistent with fMRI research which reported comparable behavioural performances in children aged 8-18 with ASD on a visual search task compared to TD controls, but increased frontal-occipital connectivity and intra-occipital connectivity in the ASD group (Keehn, Shih, Brenner, Townsend, & Muller, 2013); suggesting compensatory mechanisms may be at play in children with ASD. In contrast, the current findings conflict somewhat with recent research by (Iarocci & Armstrong, 2014) who reported decreased accuracy in children with ASD on a computerised conjunctive visual search task, but no significant interaction between age (7-9 vs. 10-12 years) and group (ASD vs. TD); with both groups demonstrating a similar pattern of improved performance with increasing age. It is possible that methodological differences, including differences in the selective attention measure utilised, may explain disparate findings between studies. Given all participating children in the current study reached ceiling for ‘targets detected’, and few errors were made by older children in either diagnostic group, it is also possible that the WATT Selective attention search task may not be challenging enough to detect overall group differences.

Differentiating Children with ASD based on Attentional Performance

Regression analyses within each age group revealed that after accounting for all other attention variables, only the switching and sustained subtests from the WATT were significant predictors of ASD diagnosis; with the switching task a significant contributor for younger children, and the sustained task a significant contributor for older children. None of the ANT-C attention network scores nor ‘false alarms’ from the selective task made a
significant contribution to either model; suggesting the WATT switching and sustained attention subtests are simply more sensitive, and thus may serve as more useful screening and/or research tools for attentional problems in children with ASD.

**Limitations**

Study limitations include the inclusion of several children within our ASD group who were taking stimulant medication, which may have impacted their performance on tasks. In addition, confirmation of clinical diagnosis was not performed via the commonly used ADI-R or ADOS. Finally, the findings of the current study should be considered in light of the cross-sectional design, and reduced sample size for age comparisons.

**Conclusion and clinical implications**

In summary, the current study examined age-related changes in the development of the alerting, orienting, and executive control networks, alongside switching, selective, and sustained attention in school-age children with and without ASD. The findings highlight the importance of considering developmental trajectories in this age group when examining attentional processes and the need for interventions targeted at specific attentional processes in children with ASD, of particular ages. Analysis of the ANT-C and WATT together suggests that the false alarm measure from the switching and sustained attention subtests from the WATT are more sensitive to the attentional problems experienced by younger and older children with ASD, and thus may serve as appropriate screening tools for ASD-related attentional problems. However, the ANT-C may serve as a useful tool for detecting subtle breakdowns in select components of attentional processing. Identification of these covert and more subtle breakdowns in attentional processing provides useful information for the future development of ASD-specific cognitive training programs, within which the ANT-C and WATT would serve as useful outcome measures to track attentional improvements. The
sensitivity of the WATT switching subtest for the detection of attentional difficulties in younger children is also promising, with potential use as an outcome measure by which to assess the effectiveness of targeted early treatment and intervention programs.

In addition, this characterisation of the unique attentional profile of children with ASD without ID may also serve to help differentiate children with ASD from other disorder groups, such as children with ADHD, with whom they share a similar behavioural attentional profile. Future research examining the development of these networks and attentional subtypes at each age across the school and into adolescence years, in larger samples, and in comparison to other developmental disorder groups such as ADHD, would be helpful to further understand the breakdown and development of these attentional processes in children with ASD.
References


Monash University

Declaration for Thesis Chapter 5

Declaration by candidate

In the case of Chapter 5, the nature and extent of my contribution to the work was the following:

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<th>Nature of contribution</th>
<th>Extent of contribution (%)</th>
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<tr>
<td>Study design, data collection, data analysis, interpretation of results, preparation of manuscript</td>
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The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

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<tr>
<td>Miss F. Fletcher</td>
<td>Study design, data collection, data analysis, interpretation of results, feedback on prepared manuscript</td>
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<tr>
<td>Dr R. Conduit</td>
<td>Study design, interpretation of results, feedback on prepared manuscript</td>
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<tr>
<td>Prof K. M. Cornish</td>
<td>Study design, interpretation of results, feedback on prepared manuscript</td>
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The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate’s and co-authors’ contributions to this work.

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CHAPTER 5

THE RELATIONSHIP BETWEEN SLEEP & ATTENTION IN SCHOOL-AGE CHILDREN

Preamble to Paper 3

The previous chapters of this thesis have characterised the cross-sectional sleep and attentional profiles of children with and without Autism Spectrum Disorder (ASD). Children with ASD were found to not only display more difficulty in objectively-measured sleep initiation and reduced total sleep duration, but also presented with more parent-reported behavioural attention problems, and pronounced difficulties on tests of sustained and switching cognitive attention. The current chapter builds on these findings, and significant gaps in the existing literature (see Chapter 2), by examining whether aspects of children’s sleep profiles are associated with their attentional profiles. In doing so, interesting associations between children’s habitual sleep quality and attentional functioning are revealed.


Note: This paper has been submitted to the Journal of Research in Autism Spectrum Disorders

Abstract

Inadequate sleep has been linked to reduced functioning in a number of key neurobehavioural areas including attention. The current study sought to explore associations between key aspects of children’s objective sleep profiles and aspects of both behavioural and cognitive attention in 34 school-aged children with Autism Spectrum Disorder (ASD) without intellectual disability, and 34 age-and-gender-matched typically-developing (TD) children; using fourteen nights of actigraphy monitoring, the Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Scale (SWAN), and objective tests of switching and sustained attention. Whilst indicators of children’s sleep quality were found to have associations with aspects of behavioural attention for both ASD and TD children, sleep fragmentation was associated with worse sustained attention in TD children only. No associations were observed between sleep duration and aspects of either behavioural or cognitive attention for either group. These findings suggest that it is the quality, not duration, of children’s habitual sleep patterns that has more impact on subsequent attentional functioning, and that, contrary to expectations; the increased severity of sleep difficulties observed in ASD does not appear to drive the increased dysfunction observed in attentional functioning.

Keywords: Autism Spectrum Disorder, School-aged children, Actigraphy, Attention, Hyperactivity, Sustained Attention, Switching Attention,
Sleep is a repetitive and active process shown to play a fundamental role in human behaviour and neurocognitive function (Barone & Krieger, 2015). The importance of sleep is particularly emphasised in paediatric populations, in which inadequate sleep has been linked to reduced executive functioning (Sadeh, Gruber, & Raviv, 2002), impaired memory (Sadeh et al., 2002), increased behavioural problems (Simola, Liukkonen, Pitkaranta, Pirinen, & Aronen, 2014), emotional disturbance (Becker, 2014; Gruber, Cassoff, Frenette, Wiebe, & Carrier, 2012; Simola et al., 2014), and overall reductions in school and academic performance (Becker, 2014). In addition, converging evidence also supports a relationship between sleep and attentional functioning (Becker, 2014; Sadeh et al., 2002; Touchette et al., 2007); with sleep hypothesised to maintain the functional integrity of frontal-parietal networks underlying aspects of cognitive attention (Astill, Van der Heijden, Van Ijzendoorn, & Van Someren, 2012). Further investigation into the relationship between these two constructs in paediatric populations is considered particularly pertinent, with attention considered integral to children’s ability to take in and learn new information.

Despite research highlighting the fundamental importance sleep plays in children’s overall maturation, growth, and physical and cognitive health, research indicates a rapid and consistent decline in the duration of sleep obtained by children and adolescents over the last 100 years (Matricciani, Olds, & Petkov, 2012). In addition to this overall decline in sleep duration, rates of sleep problems are reported to affect up to 50% of neuro-typical school-age children, and to occur at a disproportionally high rate in school-age children with Autism Spectrum Disorder (ASD); with parent-reported prevalence rates of up to 81% (Hodge, Carollo, Lewin, Hoffman, & Sweeney, 2014). The types of sleep problems experienced by children with ASD are wide-ranging in nature and include disturbances in the quality (Couturier et al., 2005; Hodge et al., 2014; Hoffman, Sweeney, Gilliam, & Lopez-Wagner,
The Relationship between Sleep & Attentional Functioning

Attention is a complex multidimensional construct which can be subdivided into overt behavioural components, such as staring into space and distractibility, as well as underlying cognitive components, which guide how well information is attended to and processed (Cornish & Wilding, 2010). In order to explore the impact sleeping well has on both these components of attention it is also important to draw the distinction between sleep quality and sleep duration. Sleep duration is typically defined as the total period of time an individual spends asleep either across the 24 hour period or during the nocturnal sleep episode, whilst sleep quality integrates several aspects of sleep including sleep initiation, maintenance of sleep (e.g. the occurrence of nocturnal awakenings), and an individual’s experience of refreshment upon awakening (Kline, 2013).

Research investigating the impact of sleep duration on behavioural aspects of attention (e.g. inattentive and hyperactive behaviours) in TD children has found that one week of restricted sleep (eight hours in bed for children in Grades 1 or 2, and six and a half hours in bed for children in Grade 3 and above) is significantly associated with increased ratings of teacher-reported attention problems in children aged 6-12 years (Fallone, Acebo, Seifer, & Carskadon, 2005), a single night of significantly restricted sleep (four hours in bed)
is significantly associated with the increased occurrence of inattentive but not hyperactive behaviours in children aged 8-15 years (Fallone, Acebo, Arnedt, Seifer, & Carskadon, 2001), and shorter polysomnography (PSG) measured sleep duration (over one night) in children aged 7-11 years is a significant predictor of teacher-reported inattention, but not hyperactivity (Gruber et al., 2012). Conversely, an earlier study by Gruber and colleagues found no association between actigraphy-measured sleep duration (averaged across four consecutive week nights, in children aged 7-11 years, and parent and teacher ratings of inattention or hyperactivity (Gruber et al., 2010). Research utilising objective sleep measures to explore the relationship between sleep and behavioural aspects of attention in children with ASD are limited overall, and to date, no known studies have looked at the relationship between sleep duration in association with behavioural aspects of attention in this population.

Research investigating the impact sleep duration has on cognitive components of attention in TD children also reports significant associations between the two. Specifically, whilst a single night of significantly restricted sleep (4 hours in bed) was not significantly associated with performance on a sustained attention or response inhibition task in children aged 6-12 years (Fallone et al., 2001), 30 minutes or more of extended sleep for three consecutive nights was associated with improved performance on tests of attentional capacity (digits forward memory test) and sustained attention in fourth (mean age of 9.80 years) and sixth grade children (mean age of 11.58 years), compared to children with no change in sleep duration and children who shortened their sleep by 30 minutes or more (Sadeh, Gruber, & Raviv, 2003). Similarly to behavioural attention, no known studies have examined the relationship between sleep duration and performance on tasks designed specifically to tap cognitive aspects of attention in children with ASD, however, correlation studies utilising executive tasks indicate that sleep duration may impact cognitive flexibility; with an
association seen between reduced parent-reported sleep duration and more preservations on the Wisconsin Card Sort Task (WCST) in children aged 7-14 years (Memari et al., 2013).

To date, only one known study has explored the relationship between sleep quality and behavioural attentional functioning in school-aged TD children; finding that children aged 7-12 years with more actigraphy-measured sleep fragmentation (determined by either a) an average of ≥ 3 night awakenings per night, or b) sleep percentage < 90%), and subsequently defined as ‘poor sleepers’, were also rated by parents as having more ‘total behaviour problems’ than ‘good sleepers’ on the Child Behaviour Checklist (CBCL) but not more difficulty with behavioural attention specifically (Sadeh et al., 2002). More research has been conducted in ASD populations; with parent–defined poor sleepers aged 2-18, and children aged 1-15 years with ASD and higher sleep disturbance scores (reflecting both reduced sleep duration and sleep quality) found to have more problems with inattention (Goldman et al., 2011; Goldman et al., 2009; Mayes & Calhoun, 2009) and hyperactivity (Goldman et al., 2011; Goldman et al., 2009; May, Cornish, Conduit, Rajaratnam, & Rinehart, 2015; Mayes & Calhoun, 2009). In addition, Goldman and colleagues also report a significant association between actigraphy-measured ‘wake after sleep onset’ (WASO; measured over two nights) and parent-ratings of hyperactivity in children with ASD without ID aged 4-10 years (Goldman et al., 2009).

Research investigating the relationship between sleep quality and cognitive aspects of attention in both TD and ASD paediatric populations is significantly limited. In terms of TD children, Sadeh and colleagues report that children aged 7-12 years with more actigraphy-measured fragmented sleep also perform more poorly on a continuous performance sustained attention task than children defined as “good sleepers” (Sadeh, Gruber, & Raviv, 2002),
whilst subjective sleep measurement in school-age children with ASD with and without comorbid ID reports no association between children’s total sleep disturbance scores and working memory ability (as indicated by the WISC-IV working memory index; Mayes & Calhoun, 2009).

Taken together these studies suggest that sleep plays some role in children’s attentional functioning. Whilst experimental research in school-age TD children supports links between sleep duration and aspects of both behavioural inattention and cognitive attention (i.e. sustained attention, response inhibition, and attentional capacity), the impact natural variations in children’s sleep length and sleep quality may have on these attentional constructs is unknown. In addition, whilst children with ASD are known to experience both sleep and attentional difficulties at significantly high rates, few studies to date have investigated the association between these constructs, in this population. Specifically, whilst increased sleep disturbance has been found to be associated with parent-reported behavioural aspects of attention, the relationship between sleep duration and behavioural attention, and between sleep (both duration and quality) and specific aspects of cognitive attention, remains unexamined in children with ASD.

The goal of the current study was, therefore, to investigate whether school-age children’s objectively-measured sleep profiles were associated with their behavioural and/or cognitive attentional functioning, and, explore whether these associations differ between TD children and children with ASD. The first aim was to investigate whether actigraphy-measured sleep length or sleep quality is associated with parent-reported ratings of behavioural inattention or hyperactivity. It is hypothesised that actigraphy-measured sleep duration will be associated with ratings of inattention whilst indicators of reduced sleep
quality (more night wakings and reduced sleep efficiency) will be associated with ratings of hyperactivity. The second aim is to explore whether sleep length or actigraphic indicators of sleep quality are associated with objectively-measured switching or sustained attention. It is hypothesised that shorter sleep duration and more fragmented sleep (e.g. more night wakings) will be associated with reduced performance on a test of sustained attention and that reduced sleep duration will also be associated with more errors on a test of switching attention. The third aim is to investigate whether any observed relationships between objectively-measure sleep and attentional functioning differ between TD children and children with ASD.

Method

Participants

The study sample consisted of 34 matched pairs: 34 individuals with a clinical diagnosis of Autistic Disorder, Asperger’s Disorder, or ASD, and 34 gender-matched TD children. All children met the following inclusion criteria: age 6;0-12;11 years; English as a first language; and full-scale IQ (FSIQ) >70. Children were excluded from both groups if they had a diagnosed seizure disorder, any medical conditions that significantly impacted hearing, vision, or motor control, or any parent-reported history of sleep disordered breathing or restless leg syndrome. Children were recruited via Melbourne-based public primary schools, webpage advertisements, and Victorian-based community centres and print media. Children in the ASD group were additionally recruited through several Victorian-based ASD services including the Asperger Syndrome Support Network Victoria, AMAZE, the Melbourne Children’s Clinic, speech therapy clinics and parent-support groups.
Children in the ASD group were tested between August 2012 and August 2013. All clinical diagnoses were completed prior to children’s participation in the current study by either a paediatrician or registered psychologist. These diagnoses were completed independent from the current research project and based on comprehensive multidisciplinary diagnostic assessments performed by clinicians at child paediatric or psychology clinics. Diagnostic reports were obtained for each child in the ASD group and checked against the DSM-IV-TR symptom checklist by the first author to ensure criteria for either autism or Asperger’s syndrome was met.

TD children were drawn from a larger sample of 95 children tested between July 2012 and August 2014 from the Monash University ‘Networks of Attention and Paediatric Sleep’ (NAPS) project. TD children were considered eligible for matching purposes if they did not have a sibling with a diagnosis of ASD, obtained a T-score below 75 on the Social Responsiveness Scale, were without any formal diagnoses, were tested outside of school holidays, and had at least 11 nights of actigraphy and corresponding sleep diary data.

**Measures**

*Demographics and Medical History*

Demographic information (gender, age) and medical history (medication, medical problems, formal diagnoses, history of sleep difficulties, and history of learning difficulties/language delays) were obtained from parents using a semi-structured interview during initial screening and via diagnostic reports. Socio-economic information including child ethnicity and parent education were obtained using a brief questionnaire. A socioeconomic status (SES) score, indicating relative socio-economic advantage/disadvantage, was calculated for each participant based on their residential postcode using the
Socio-economic Indexes for Areas data from the Australian Bureau of Statistics, which allocates each area a decile number ranging from 1 to 10 where 1 indicates the most disadvantaged, and 10 indicates the most advantaged area (Australian Bureau of Statistics, 2013).

**Intellectual Functioning**

All participating children were administered the two-subtest version (vocabulary and matrix reasoning) of the *Wechsler Abbreviated Scale of Intelligence* (WASI; Wechsler, 1999). This measure is normed for use with individuals aged 6-89 years and yields a full-scale intelligence quotient (FSIQ) comparable to the *Wechsler Intelligence Scale for Children – Third Edition* (WISC-III; Wechsler, 1991) FSIQ. Intercorrelations between FSIQ scores derived from the two and four subtest versions of the WASI range from .91 to .97 (Wechsler, 1999).

**Autistic Symptoms**

All parents completed the *Social Responsiveness Scale* (SRS) designed to measure social impairment associated with ASD (Constantino & Gruber, 2005). This 65-item questionnaire is normed for use in children aged 4 to 18 years. Items are rated on a three-point Likert scale where 0 is “never true” and 3 is “almost always true”, based on the child’s behaviour during the previous six months. The questionnaire yields a total score (ranging from 0 to 195), which can be converted to a T-score and provides an indicator of the severity of social impairment, and five subscales: social awareness, social communication, social motivation, social cognition, and autistic mannerisms. T-scores ≥75 have been found to discriminate children with and without ASD with specificity and sensitivity values of .75 and
.85, respectively (Constantino et al., 2003) and correlations between SRS scores and Autism Diagnostic Interview-Revised domain scores range from .65 to .77 (Constantino et al., 2003).

*Sleep Assessment*

Children’s sleep-wake patterns were assessed over a 14-15 night period via actigraphy monitoring. The current study utilised the Actiwatch-2 (Respironics, USA), a self-contained micro-computer weighing approximately 16 grams. Children were instructed to wear the actigraphs on their non-dominant wrist, day and night, over the 14-15 day period (with instruction to remove prior to immersion in water or other activities in which the watch may be damaged). The actigraphs contained a marker button which children and parents were instructed to press to indicate bedtime and get-up time, an integrated light sensor (range 400-900 nm), and a solid state piezo-electric accelerometer with a sampling rate of 32 Hz and a non-volatile memory of 1Mbit. The actigraphs collected data in 30second epochs and data analysis set at a medium sensitivity threshold (i.e. 40 activity counts per epoch required to be scored as ‘wake’).

Marker button presses, activity counts per epoch, and light information were stored in the actiwatch memory and later downloaded to the Respironics Actiware Software (Version 5.70.1). These settings have been validated against PSG, providing an agreement rate of 87.3%, sensitivity of 93.9% and a specificity of 59.0% (note that despite the low specificity, overall wake time was not significantly different to PSG wake time) for PSG total sleep, wake times, and sleep efficiency (Hyde et al., 2007). A ten-minute immobility rule was applied for the scoring of sleep onset time, recently cited as the most appropriate for the use of the Actiwatch-2 in school-aged children (Meltzer, Walsh, & Peightal, 2015). Bedtime and get-up time were manually scored in accordance with marker button presses in conjunction
with parental sleep diaries (Meltzer, Montgomery-Downs, Insana, & Walsh, 2012). As the most widely used definition for nocturnal wake frequency, night wakings (NW) were manually scored as 10 or more consecutive epochs (i.e. 5 minutes) of wake in between sleep-onset time and sleep-offset time (Meltzer et al., 2012). Five additional actigraphy variables were autoscored by the Respironics software which covered timing, sleep duration, sleep initiation, and overall sleep efficiency.

Parents were asked to maintain a sleep-wake diary throughout their child’s participation. Parents indicated bedtime, time of sleep onset, time and duration of night awakenings, time of sleep offset, get-up time, daytime naps, and any time the actiwatch was removed. If a parent indicated that the child had an unusual night of sleep (e.g. sleepover, illness) this night was excluded from analysis.

**Attention Measures**

The *Strengths and Weakness of ADHD symptoms and Normal Behavior scale* (SWAN; Swanson et al., 2006) is a caregiver-completed measure of ADHD. The SWAN consists of 18 items based on the 18 symptoms of ADHD listed in the DSM-IV-TR (American Psychiatric Association, 2000). Items 1-9 make up the Attention Deficit subscale and items 10-18 make up the Hyperactivity/Impulsivity subscale. Unlike other commonly used measures of ADHD behaviour, items are phrased relative to normal, not abhorrent behaviour expectations and rated on a seven-point scale which ranges from ‘far below average (0) to ‘far above average’ (6). Lower scores on each subscale, therefore, indicate higher levels of ADHD symptomology. It shows comparable validity, reliability, and heritability to the well-validated Disruptive Behavior Rating Scale, and shows good ability to
capture sufficient variance at both ends of the inattention and hyperactivity-impulsivity spectrum (Arnett et al., 2013).

The Wilding Attention Test for Children (WATT; Wilding, Munir, & Cornish, 2001). The WATT consists of experimental Vigilant and Visual Search tasks designed to measure different aspects of cognitive attention in children aged 4 to 16 years. Each task consisted of a screen display of various shapes ("holes") of differing colours and sizes, on a green background.

The dual-target visual-search condition (Visearch-dual) was used to assess attentional switching/executive control of attention. Stimuli consisted of 30 targets (15 black vertical ellipses and 15 brown horizontal ellipses) and 70 distracters (black horizontal ellipses, black circles, brown horizontal and vertical ellipses, brown circles, and large green ellipses containing small brown rectangles). Children were instructed to switch between clicking on "black ovals standing up" followed by "brown ovals on their side", and to continue switching between the two types of holes, as fast as possible, until they had found the "king monster." Black vertical ellipse targets revealed small blue monsters, brown horizontal ellipse targets small yellow monsters. The king monster always appeared at the 20th target. If the participant was unable to find the king after 50 responses the condition terminated.

The Vigilan visual-search task was employed in order to assess sustained/alerting attention. Children were instructed to search the "whole forest" (screen) and click on "holes" as quickly as possible if a yellow ring appeared around them, as this indicates a monster is hiding there until they find the king. The yellow ring appeared around black vertical ellipses at irregular intervals of between 4-14 seconds. Rings would remain around targets for 7
seconds before disappearing. If children clicked on targets within 7 seconds a small monster would appear. The king monster always appeared at the 14\textsuperscript{th} target. If the participant was unable to locate and click on 14 targets within 4 minutes the condition terminated.

**Procedure**

Upon initial conduct by the parent or guardian, initial screening was conducted over the telephone and/or via email in order to ascertain whether the child met eligibility criteria. Children were tested on two separate occasions, exactly 14–15 days apart, either within the participant’s home or at the Monash University Child and Adult Development Laboratory. The first preliminary testing session consisted of obtaining informed written consent from parents, distribution of parent questionnaires (SWAN, SRS), actigraphs, and sleep diaries, and administration of the WASI. At the second testing session parents returned completed questionnaires, actigraphs and sleep diaries, and children completed assessments of cognitive attention. For both sessions, children were seen individually in a quiet room. Children completed a practice trail for the Vigilan condition but not for Visearch-dual.

**Data Analysis**

Comparisons between the ASD and TD groups for categorical and continuous demographic and clinical characteristic variables were accomplished using $\chi^2$ analysis and T-tests. Comparisons between groups for the WATT selective and sustained cognitive attention variables were accomplished using Mann-Whitney U test, as data was abnormally distributed. Within-group correlational analysis was in order to assess whether key actigraphic sleep variables (sleep duration, sleep onset latency, sleep efficiency, and number of night wakings) were significantly associated with subjective behavioural ratings (SWAN inattention and hyperactivity/impulsivity), and objective cognitive measurement, of children’s attention, and
subsequent hierarchical regression analyses employed where significant correlations were found. All regression analyses included an interaction term in order to determine whether any relationship between the dependent variable and predictor sleep variable of interest were moderated by group (ASD vs TD). In Step 1, the actigraphy variable of interest and group term was entered. In Step 2, the interaction term between the centered actigraphy variable and group was entered.

Results

Sample Characteristics

The demographic and clinical characteristics of children with ASD and their TD controls are presented in Table 1. No significant differences were seen between the ASD and TD group for chronological age, gender, ethnicity, or calculated SES score. As expected the ASD group were rated significantly higher on measures of social impairment, $t(52.58) = 14.98, p < .001$, inattention, $t(59.63) = -8.55, p < .001$, and hyperactivity/impulsivity, $t(65) = 7.84, p < .001$, whilst the TD group displayed significantly higher FSIQ scores, $t(66) = -7.73, p < .001$. 
Table 1. Descriptive Statistics for Demographic and Clinical Characteristics by Group

<table>
<thead>
<tr>
<th></th>
<th>ASD (n=34)</th>
<th>TD (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (months) M (SD)</strong></td>
<td>106.65 (24.49)</td>
<td>106.88 (22.15)</td>
</tr>
<tr>
<td><strong>Gender males (females)</strong></td>
<td>23 (11)</td>
<td>23 (11)</td>
</tr>
<tr>
<td><strong>FSIQ M (SD)</strong></td>
<td>99.53 (13.87)</td>
<td>112.53 (14.33) ***</td>
</tr>
<tr>
<td><strong>Ethnicity n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>32 (94.1)</td>
<td>27 (79.4)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (5.9)</td>
<td>6 (17.6)</td>
</tr>
<tr>
<td><strong>SES Score M (SD)</strong></td>
<td>7.71 (2.14)</td>
<td>7.62 (2.50)</td>
</tr>
<tr>
<td><strong>SRS Score M (SD)</strong></td>
<td>96.71 (25.31)</td>
<td>21.74 (14.51) ***</td>
</tr>
<tr>
<td><strong>SWAN Inattention M (SD)</strong></td>
<td>15.44 (9.33)</td>
<td>32.24 (6.65) ***</td>
</tr>
<tr>
<td><strong>SWAN Hyperactivity/Impulsivity M (SD)</strong></td>
<td>17.24 (8.69)</td>
<td>32.97 (8.09) ***</td>
</tr>
</tbody>
</table>

FSIQ: Full-Scale Intelligence Quotient; SES: Socioeconomic Score; SRS: Social Responsiveness Scale; SWAN: Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Scale

***significant at $p \leq .001$,

Group Differences on Cognitive Attention Measures

Group differences in children’s performances on the WATT selective and sustained attention tasks were assessed using the Mann-Whitney U Test. In terms of the selective attention children with ASD were observed to make significantly more false alarms, $U = 284.00, p = .001$, and make significantly fewer hits than TD children, $U = 438.00, p = .016$. Children with ASD were also observed to make more false alarms than TD children on the sustained attention task, $U = 352.50, p = .032$, but made a similar number of total hits, $U = 399.50, p = .131$. 
### Table 2. Group Differences on Measures of Selective and Sustained Attention

<table>
<thead>
<tr>
<th></th>
<th>ASD</th>
<th>TD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Switching Attention</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>False Alarms</td>
<td>13.88 (12.92)</td>
<td>3.74 (4.25)***</td>
</tr>
<tr>
<td>Total Hits</td>
<td>19.40 (1.29)</td>
<td>19.97 (0.17)*</td>
</tr>
<tr>
<td><strong>Sustained Attention</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>False Alarms</td>
<td>8.39 (7.81)</td>
<td>5.00 (5.62)*</td>
</tr>
<tr>
<td>Total Hits</td>
<td>7.58 (4.28)</td>
<td>9.18 (3.42)</td>
</tr>
</tbody>
</table>

*significant at $p \leq .05$, ***significant at $p \leq .001$

### Associations between Actigraphic Sleep and Behavioural Attention

Examination of correlations between chronological age and behavioural attention showed that for both groups age did not significantly correlate with children’s inattention [ASD: $r(33) = -.154, p = .39$; TD: $r(33) = .057, p = .753$] or hyperactivity, [ASD: $r(33) = -.261, p = .135$; TD: $r(33) = -.009, p = .960$] scores.

Examination of the associations between key actigraphic sleep variables and behavioural attention showed that sleep onset latency was significantly positively correlated with parent ratings of inattention in the TD group, $r(34) = .430, p = .011$, and with hyperactivity ratings in the ASD group, $r(33) = .373, p = .033$. Sleep efficiency was negatively associated with inattention in the TD group, $r(34) = -.405, p = .017$, and hyperactivity ratings in the ASD group, $r(33) = -.428, p = .013$. No significant associations were seen between actigraphic variables of sleep duration, duration of night waking’s, and number of night waking’s and parent ratings of inattention or hyperactivity for either group (all $ps < .05$). In light of significant correlations, subsequent hierarchical regression analysis
was employed in order to assess whether sleep onset latency and sleep efficiency were able to predict subjective ratings of inattention and/or hyperactivity.

In terms of SOL and inattention, Step 1 of the hierarchical regression showed that group and SOL accounted for a significant 57% of variance in children’s inattention scores, $R^2 = .57$, $F (2, 64) = 41.49$, $p < .001$, with both group and SOL significantly associated with children’s inattention scores (see Table 3). Step 2 did not account for a significant increase in variance, $R^2$ change = .013, $F$ change (1, 63) = 1.87, $p = .18$, indicating no interaction between group and SOL in association with children’s inattention scores.

For SOL and hyperactivity, Step 1 of the hierarchical regression showed that group and SOL accounted for a significant 53% of variance in children’s hyperactivity scores, $R^2 = .53$, $F (2, 64) = 36.40$, $p < .001$, with both group and sleep efficiency significantly associated with children’s hyperactivity scores (see Table 4). Step 2 did not account for a significant increase in variance, $R^2$ change = .000, $F$ change (1, 63) = .03, $p = .87$, indicating no interaction between group and sleep efficiency in association with children’s hyperactivity scores.

Table 3. Unstandardised (B) Regression Coefficients for Each Predictor Variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>Inattention</th>
<th>Hyperactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$B$</td>
<td>$t$</td>
</tr>
<tr>
<td><strong>Step 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Centered SOL</td>
<td>.10</td>
<td>2.07</td>
</tr>
<tr>
<td>Group</td>
<td>-18.15</td>
<td>-9.11</td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interaction term (Group x SOL Centered)</td>
<td>-.18</td>
<td>-1.37</td>
</tr>
</tbody>
</table>

*significant at $p \leq .05$, ***significant at $p \leq .001$
Step 1 of the hierarchical regression investigating the relationship between inattention and sleep efficiency was significant, $R^2 = .56$, $F (2, 64) = 41.03, p < .001$, with group ($p < .001$), but not sleep efficiency ($p = .054$) significantly associated with children’s inattention scores. Step 2 did not account for a significant increase in variance, $R^2$ change = .008, $F$ change $(1, 63) = 1.17, p = .28$, indicating no interaction between group and sleep efficiency in association with children’s inattention scores.

For sleep efficiency and hyperactivity, Step 1 of the hierarchical regression showed that group and sleep efficiency accounted for a significant 54% of variance in children’s hyperactivity scores, $R^2 = .54$, $F (2, 64) = 37.21, p < .001$, with both group and sleep efficiency significantly associated with children’s hyperactivity scores (see Table 4). Step 2 did not account for a significant increase in variance, $R^2$ change = .003, $F$ change $(1, 63) = .36, p = .55$, indicating no interaction between group and sleep efficiency in association with children’s hyperactivity scores.

**Table 4.** Unstandardised ($B$) Regression Coefficients for Each Predictor Variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hyperactivity-Impulsivity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$B$</td>
</tr>
<tr>
<td><strong>Step 1</strong></td>
<td></td>
</tr>
<tr>
<td>Mean Centered Sleep Efficiency</td>
<td>-76.10</td>
</tr>
<tr>
<td>Group</td>
<td>17.35</td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td></td>
</tr>
<tr>
<td>Interaction term (Group x Sleep Efficiency Centered)</td>
<td>-37.34</td>
</tr>
</tbody>
</table>

*significant at $p \leq .05$, ***significant at $p \leq .001$

**Associations between Actigraphic Sleep and Cognitive Attention**

Given that mean scores for total hits for the TD group were around ceiling on the switching attention task, only children’s false alarms scores on this task were analysed in
relation to their relationship with sleep. Pearson correlations revealed a significant negative correlation between age and number of false alarms made on the switching attention task for the ASD group only [ASD: \( r(32) = -.512, p = .003 \); TD: \( r(34) = -.265, p = .130 \)]. For sustained attention, age was significantly correlated with number of hits made in both groups [ASD: \( r(31) = .632, p < .001 \); TD: \( r(33) = .478, p = .005 \)], but not with number of false alarms [ASD: \( r(31) = .155, p = .405 \); TD: \( r(33) = -.142, p = .432 \)].

Partial correlations, controlling for age, revealed no significant associations between and any actigraphic sleep variables and number of errors (false alarms) made on the switching attention task or total number of hits made on a test of sustained attention for either the ASD or TD group (all \( p < .05 \); see Table 5). Pearson bivariate correlations examining associations between key sleep variables and number of errors made on a test of sustained attention, however, revealed a significant positive association between average duration of night waking’s and number of false alarms for the TD group only, \( r(33) = .352, p = .044 \). In light of this significant association, a subsequent hierarchical regression analysis was employed in order to assess whether the average duration of children’s night waking’s was able to predict poorer sustained performance (i.e. more false alarm errors), and, whether this relationship varied as a function of group.

Step 1 of the hierarchical regression showed that group and duration of night wakings did not account for a significant percentage of variance in the number of false alarms errors children made on the sustained attention task, \( R^2 = .074, F (2, 61) = 2.44, p = .095 \). In addition, Step 2 did not account for a significant increase in variance, \( R^2 \) change = .10, \( F \) change (1, 60) = 1.88, \( p = .18 \), indicating no interaction between group and duration of night wakings in association with children’s sustained attention error rates. No other significant
associations were seen between any other actigraphic sleep variables and number of errors made on the sustained attention task for either group (all $p s < .05$).

**Table 5.** Pearson’s correlations between key actigraphic variables and measures of switching and sustained attention for the ASD (above the diagonal) and TYP (below the diagonal) groups

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6*</th>
<th>7*</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. SD Total</td>
<td>1</td>
<td>-.416*</td>
<td>.420*</td>
<td>.237</td>
<td>.310</td>
<td>-.231</td>
<td>-.053</td>
<td>.198</td>
</tr>
<tr>
<td>2. SOL Total</td>
<td>-.563**</td>
<td>1</td>
<td>-</td>
<td>-.105</td>
<td>-.122</td>
<td>-.031</td>
<td>.028</td>
<td>.064</td>
</tr>
<tr>
<td>3. SE Total</td>
<td>.574***</td>
<td>-</td>
<td>1</td>
<td>-.229</td>
<td>-.166</td>
<td>.088</td>
<td>.104</td>
<td>-.114</td>
</tr>
<tr>
<td>4. NW No. Total</td>
<td>.170</td>
<td>-.262</td>
<td>-.143</td>
<td>1</td>
<td>.939***</td>
<td>-.063</td>
<td>-.261</td>
<td>.001</td>
</tr>
<tr>
<td>5. NW Dur Total</td>
<td>.158</td>
<td>-.191</td>
<td>-.233</td>
<td>.964***</td>
<td>1</td>
<td>-.101</td>
<td>-.184</td>
<td>-.006</td>
</tr>
<tr>
<td>6. Switching Errors*</td>
<td>-.063</td>
<td>-.092</td>
<td>.021</td>
<td>-.072</td>
<td>-.065</td>
<td>1</td>
<td>-.250</td>
<td>-.220</td>
</tr>
<tr>
<td>7. Sustained Hits*</td>
<td>-.148</td>
<td>.195</td>
<td>-.078</td>
<td>-.228</td>
<td>-.083</td>
<td>.007</td>
<td>1</td>
<td>-.138</td>
</tr>
<tr>
<td>8. Sustained Errors</td>
<td>.021</td>
<td>-.203</td>
<td>-.156</td>
<td>.284</td>
<td>.352*</td>
<td>.199</td>
<td>-.437*</td>
<td>1</td>
</tr>
</tbody>
</table>

*significant at $p \leq .05$, **significant at $p \leq .01$, ***significant at $p \leq .001$, *partial correlations controlling for age

**Discussion**

The current study assessed whether associations exist between objectively-measured sleep and attentional functioning in school-age children with and without ASD. Whilst correlation analyses did not support an association between children’s average actigraphy-measured sleep duration and behavioural attention (inattention or hyperactivity), significant associations were seen between behavioural attention ratings and indicators of sleep quality, although not in the direction expected based on previous research. Contrary to hypotheses, no association was seen between actigraphy-measured sleep duration and sustained or switching attention, however, as hypothesised, greater sleep fragmentation was associated with worse sustained attention; although this relationship was only evident in TD children.
The results of the present study indicate that it is the quality of children’s sleep, not duration, which has a greater impact on behavioural attention functioning in school-age children with and without ASD. The significant associations seen between sleep onset latency and ratings of inattention and hyperactivity conflict with sleep research conducted in children with Attention-Deficit/Hyperactivity-Impulsivity Disorder (ADHD); in which sleep onset difficulties have been found to be prominent (Cortese, Faraone, Konofal, & Lecendreux, 2009). Specifically, whilst it is hypothesised that the high prevalence of sleep onset problems observed in children with ADHD is due to the behavioural problems inherent to the disorder, such as hyperactivity; resulting in increased settling difficulties and bedtime resistance (Gruber, Fontil, Bergname, Amsel, Frenette, & Carrier, 2012), this hypothesis would not account for associations seen in the current study; in which reduced, not increased difficulties with inattention and hyperactivity, were associated with longer SOL in TD and ASD participants, respectively. This observed discrepancy in the direction of the relationship between SOL and hyperactive behaviour seen in children with ASD suggests that different brain mechanisms may be driving the hyperactive behaviour problems observed in ASD, and/or that increased levels of daytime activity may simply lead to more fatigue in children with ASD than children ADHD. Future research investigating other potential mechanisms for sleep initiation difficulties in ASD is clearly warranted, and the inclusion of an ADHD group alongside TD controls recommended, in order to disentangle the complex relationship which appears to exist between sleep initiation and behavioural attention/inattention. Whilst our hypothesis that indicators of sleep quality rather than sleep duration would also be associated with ratings of hyperactivity was supported, similarly to that observed for SOL, the relationship between sleep efficiency and behavioural attention measures was in the opposite direction to that expected; with increased sleep efficiency associated with worse attention in
TD children and increased levels of hyperactivity in ASD. It is possible that the previously described relationship between SOL and behavioural attention scores may also be driving these associations.

Contrary to our hypothesis, no significant association was observed between children’s average actigraphic sleep duration and behavioural ratings of inattention. This finding is inconsistent with experimental research studies in which restrictions/extensions in sleep duration were found to impact ratings of behavioural inattention (Fallone et al., 2001; Fallone et al., 2005), and observational research based on a single night’s sleep in which shorter PSG-measured sleep duration was found to predict more inattentive behaviour (Gruber et al., 2012). The current finding is however in line with previous actigraphic research conducted by Gruber and colleagues, who also looked at average sleep duration across numerous nights in school-age children (Gruber et al., 2010). These findings not only emphasise the importance of obtaining an accurate measurement of children’s habitual sleep profile, rather than a snapshot, in order to assess its influence on subsequent functioning, but also suggest that sleep duration may have less impact on behavioural inattention in school-age children with and without ASD without a diagnosed sleep condition, than previous research has indicated.

Whilst no significant associations were observed between objective measures of sleep length and performance on objective tests of switching or sustained attention, consistent with research by Sadeh and colleagues (Sadeh et al., 2002), increased sleep fragmentation was found to be significantly associated with reduced accuracy on a test of sustained attention in TD children only. The absence of any significant association within the ASD group may indicate that, despite higher reported rates of sleep problems in children with ASD (Hodge et
al., 2014; Liu et al., 2006; Souders et al., 2009), sustained attention may be more affected by poor sleep in TD children. Unlike Sadeh et al. (2002), each sleep variable in the current study was looked at continuously both within and across our ASD and TD groups. This approach allowed us to assess whether these sleep factors are having a significant impact on school-age children’s cognitive attention functioning regardless of whether they are significantly disrupted or not, and suggest that reducing factors which may be impacting the occurrence of sleep fragmentation in TD children may also result in improvements in sustained attention. The finding of no association between sleep duration and cognitive attention performance is inconsistent with previous research in TD children which reports changes in sustained attention functioning in association with manipulation of sleep length (Fallone et al., 2001; Sadeh et al., 2003), indicating that in school-age children with and without ASD, and without a diagnosed sleep disorder, average habitual sleep duration patterns have little bearing on cognitive attention functioning. Future research should instead seek to explore the impact of naturally occurring sleep duration of the previous night specifically, as well as the differences in habitual sleep variability across a typical week, on subsequent cognitive attention functioning.

The current study is limited by the relatively small sample size and subsequently reduced statistical power. As such, competing explanations for null findings should not be disregarded and replication in larger samples warranted. In addition, whilst pubertal development is known to affect both sleep and behavioural functioning, a measure of children’s pubertal stage was not included in the current study, and thus its impact on sleep and neurobehavioural functioning could not be assessed.
Together the current findings suggest that whilst school-age children’s habitual sleep quality has an impact on their subsequent behavioural attention, it appears to have little bearing on their cognitive attention functioning. While previous experimental research has strongly implicated the influence of sleep length on children’s subsequent neurobehavioural functioning, the current study suggests average habitual sleep length has little impact on either behavioural or cognitive attention in children without severe sleep issues (e.g. children without a diagnosed sleep disorder). In addition, although children with ASD are reported to experience much higher rates of sleep disturbance, and greater severity of sleep problems commonly associated with childhood, the absence of significant group interactions across the current study suggests that these increased sleep difficulties do not correspond to more impaired behavioural or cognitive attention, and thus other areas should be targeted above sleep in order to improve attentional functioning in children with ASD.
References


**CHAPTER 6**

**GENERAL DISCUSSION**

The overarching aim of this thesis was to explore differences in the subjective and objective sleep and attention profiles of school-age children (6-12 years) with Autism Spectrum Disorder (ASD) without intellectual disability (ID), compared to their typically-developing (TD) peers, and investigate the impact of sleep and sleep difficulties on attentional functioning. As Chapter 2 of the current thesis highlights, an investigation into the impact of sleep disturbance on attentional functioning in ASD has remained an underexplored area in paediatric research despite a high prevalence of sleep problems in this population, and an already compromised cognitive and behavioural system. In lieu of this gap, this thesis offers a systematic investigation into the profile of both sleep and attention in primary school-age children with ASD without comorbid intellectual disability, and explores associations between the two in order to: a) characterise the unique profile of deficits experienced by this population, and b) better understand the impact of sleep and sleep disturbance on behavioural and cognitive attention functioning. This final thesis chapter integrates the main findings
across the three studies presented in this thesis. It discusses how the present findings may be integrated to inform theory regarding the underlying aetiology of sleep problems in ASD, the nature, possible emergence, and potentially underlying mechanisms of attention dysfunction, as well as discusses their clinical implications. The discussion concludes with a discussion of study limitations and suggested directions for future research.

6.1. Overview of findings

Chapter 3, which explored differences in the sleep-wake profiles between children with ASD without ID and their age and gender-matched TD children, using fourteen nights of actigraphic monitoring and the Children’s Sleep Habits Questionnaire (CSHQ), serves to enhance our understanding of the frequency and severity of sleep disturbance in school-age children with ASD; with 91% of our ASD sample identified by parents as having a current sleep problem compared to 50% of our TD sample. Similar to previous studies, parents of children with ASD endorsed increased difficulties across multiple sleep domains; with the largest effect sizes observed for sleep duration, night waking and sleep anxiety subscales (Couturier et al., 2005; Hodge et al., 2014; Hoffman, Sweeney, Gilliam, & Lopez-Wagner, 2006; Souders et al., 2009). In addition, the concurrent use of actigraphy reinforced difficulties in the initiation of sleep as a core and persistent feature of the ASD sleep profile, as well as identifying greater between and within-child variability in sleep onset latency. Whilst the increased between-child variability likely reflects the heterogeneous nature characteristic of ASD, the finding of increased within-child variability suggests multiple and possibly interacting causes underlie the sleep initiation difficulties commonly experienced by this population.

Chapter 4 provided an investigation into the cognitive attention profile of school-age children with ASD with several important findings. Firstly younger children with ASD
experienced difficulties utilising visual cues to improve their performance on the Attention Network Test for Children (ANT-C); suggesting that they may be less receptive to the information provided in these cues. Secondly, children with ASD demonstrated developmental differences in terms of the alerting network efficiency whereby TD children showed improved use of alerting cues with older age, while the ASD group showed the inverse relationship. Finally, in addition to these more subtle breakdowns in attentional functioning, children with ASD were also observed to perform more poorly on tests of switching and sustained attention overall and demonstrated unique developmental changes on these tasks; with improvements in switching attention observed with older age whilst similar age improvements in task accuracy were not seen for sustained attention. These findings indicate that children with ASD without ID experience deficits in both the orienting and alerting attention networks over the school-age years, whilst also highlighting the importance of consideration of developmental changes over this age span. In addition, it appears that the ANT-C may not be a sensitive measure of the orienting network in this population, with the switching and sustained attention tasks from the Wilding Attention Test for Children (WATT) appearing more sensitive to the attentional problems experienced by school-age children with ASD.

Finally, Chapter 5 explored whether children’s objectively-measure sleep profiles were associated with their behavioural and cognitive attention functioning. Together, findings suggest that indicators of sleep quality (i.e. sleep onset latency, sleep efficiency) but not average sleep duration are associated with children’s behavioural attention function; however, associations observed between increased sleep efficiency and higher ratings of behavioural attention indicate that this relationship requires further disentangling. A significant association was observed between duration of night wakings in the TD group and increased errors on a test of sustained attention. No other significant associations were
observed between sleep and cognitive attention; suggesting that within our ASD group, children’s habitual sleep patterns had little bearing on their cognitive attention functioning, and are not driving the deficits observed in switching and sustained attention. In addition, this study also emphasised the importance of obtaining a measure of children’s habitual sleep profile rather than a snapshot of their sleep, as most previous studies have done.

6.2. Theoretical implications

6.2.1. Aetiology of sleep problems in children with ASD

It has been proposed that the sleep problems frequently seen in children with ASD are underlined by a complex interaction between neurobiological abnormalities, and psychological, behavioural, and social factors (Cortesi et al., 2010; Richdale & Schreck, 2009). Abnormalities in melatonin production, which plays a direct role in the regulation of the sleep-wake cycle by chemically inducing drowsiness in response to light levels (release inhibited by light and stimulated by dark; (Brzezinski, 1997), have previously been implicated, with individuals with ASD found to have elevated daytime, and decreased nocturnal melatonin levels (Kulman et al., 1999; Nir et al., 1995; Ritvo et al., 1993). In addition, behavioural factors, such as adherence to non-functional routines or rituals at bedtime are hypothesised to play a role in terms of increased bedtime resistance and settling difficulties, and commonly co-occurring psychiatric conditions such as depression, anxiety, and ADHD are proposed to interfere with sleep regulation and to impair sleep quality (Cortesi et al., 2010; Ferber, 1996; Paavonen et al., 2008; Richdale & Schreck, 2009; Tani et al., 2003).

The current study informs this model in several ways. Firstly, comparisons between sleep-medicated (melatonin) and non-sleep medicated children supports a relationship between melatonin production and time of sleep onset in children with ASD, but suggests
that factors other than abnormal melatonin production are at play in terms of the reduced sleep quality experienced; with no difference seen between medicated and non-medicated children in terms of total parent-reported sleep problems (e.g. CSHQ total scores), or actigraphic sleep-onset latency and sleep efficiency measures, despite children with ASD displaying more difficulty in these areas. Secondly, the increased between and within-child variations seen in the ASD groups sleep-onset latency suggest that the factors driving this prominent sleep difficulty in children with ASD not only differ between individuals within the disorder but that numerous dynamic and interacting causes may be at play in individuals with ASD. Finally, examination of associations between children’s objectively-measure sleep and ratings of behavioural attention revealed a surprising but significant association between higher ratings of hyperactivity and increased sleep efficiency in children with ASD. Sleep efficiency is defined as the ratio of time spent asleep to the amount of time spent in bed. As such, higher sleep efficiency scores typically reflect greater sleep quality (e.g. faster sleep initiation and less fragmented sleep). This finding conflicts with existing hypotheses which suggest that increased hyperactivity is associated with more disordered sleep in ASD; with previous research reporting associations between parent-reported sleep disturbance and increased hyperactivity (Allik et al., 2006; Goldman et al., 2011; Goldman et al., 2009; May, Cornish, Conduit, Rajaratnam, & Rinehart, 2015; Mayes & Calhoun, 2009), parent-reported sleep problems and ADHD profiles (DeVincent, Gadow, Delosh, & Geller, 2007; Goodlin-Jones, Waters, & Anders, 2009; Liu, Hubbard, Fabes, & Adam, 2006), and actigraphic sleep fragmentation and hyperactivity (Goldman et al., 2009). One possible explanation for this finding may be that children with higher levels of hyperactivity and subsequent daytime activity are simply more fatigued come bedtime and as a result, fall asleep more quickly and wake less often during the night.
6.2.2. Differences in Attentional Network Development in ASD

This thesis has revealed abnormalities in the development of both the orienting (switching attention) and alerting networks (sustained attention and vigilance) of attention in children with ASD compared with TD children. Difficulties in the orienting network in ASD were most evident in early childhood, with children with ASD demonstrating significant orienting network efficiency improvements, and/or more successful employment of compensatory mechanisms in later childhood. The presence of pronounce deficits in attentional switching during early childhood, alongside research reporting associations between early impairments in attentional disengagement and later autism diagnosis (Zwaigenbaum et al., 2005), suggests that abnormal functioning of the orienting network may represent a primary disturbance in ASD rather than an associated deficit, and in fact, as has been suggested by Keehn and colleagues, may play a role in the emergence of key features of the disorder such as impaired social communication, and repetitive activities and behaviour (Keehn, Müller, & Townsend, 2013).

In contrast to the orienting network, findings regarding the alerting network support increased dysfunction in this network compared to TD children with older age, and has further implicated abnormal frontal lobe development as a leading cause of the cognitive and functional impairments associated with ASD. Specifically, the finding of decreased efficiency in the alerting network and decreased accuracy on a test of sustained attention in later childhood is not inconsistent with previous imaging research which has documented a period of abnormally slow growth in frontal brain regions across middle to late childhood (Courchesne, Campbell, & Solso, 2011; Kosaka et al., 2010), and reduced activation of prefrontal cortical areas (Murphy et al., 2014), and is likely to have developmental consequences for a number of other domains including social and academic functioning.
6.2.3. The relationship between sleep and attention dysfunction

Associations observed between sleep and attention in the current thesis together suggest that children’s habitual sleep patterns have a greater impact on behavioural aspects of attention than the underlying cognitive components, however these relationships appear to differ as a function of group, and in some cases appear counterintuitive (e.g. increased sleep efficiency linked to increased hyperactivity and inattention). Overall, whilst findings support some relationship between children’s habitual sleep patterns and attentional functioning; this relationship is clearly complex, with other factors possibly mediating the relationship between the two. Further research in larger samples, which follows children over at least three years, and examines differences in sleep profiles between good and poor attenders, may help disentangle the relationship between these important concepts in TD and ASD populations. In addition, the potential development of more age-sensitive attention measures, which allow capture of subtle changes in children’s attentional functioning over time, may also help breakdown any interrelationships which exist between sleep and cognitive attention.

6.3. Clinical implications

The empirical studies presented in this thesis further validate the increased frequency and severity of disturbed sleep in school-age children with ASD; suggesting that uniform screening for sleep difficulties may be warranted in this population. Furthermore, our research supports subsequent assessment and evaluation in those children in which sleep difficulty is indicated using a combination of objective and subjective sleep measures. This is due to the multiple, and sometimes overlapping, sleep problems experienced by children with ASD, and the tendency for parents to identify problems across all aspects of the sleep profile rather than a prominent issue in one area which may be driving other difficulties (e.g. a prominent issue with sleep initiation driving overall reduced sleep efficiency and related
bedtime behavioural disruptions). This assessment approach would allow identification of the precise nature of sleep difficulties experienced by each individual, and the subsequent application of targeted intervention. In addition, the finding of age-related changes in children’s sleep profiles, alongside increased within and between child sleep variability, and continued sleep difficulties in children currently taking medication to aid sleep and sleep onset specifically (i.e. melatonin), also emphasises the need for the application of a personalised, age-sensitive, and multimodal approach to the management and treatment of sleep difficulties in children with ASD, rather than a blanket treatment approach (e.g. prescription of sleep medication alone).

Attention is a critical gateway to learning and if disrupted will have a deleterious impact on learning outcomes. Findings from this thesis have identified that alongside elevated levels of behavioural inattention and hyperactivity, children with ASD also experience deficits at the cognitive level of attention which are likely to have implications for both learning and behaviour. Specifically, reduced receptivity to attentional orienting cues in younger children with ASD, alongside impairments in switching attention, are likely to be expressed at a behavioural level in terms of increased rigidity and inflexibility and reduced responsiveness to environmental cues designed to help direct children to relevant information. As a result, younger children with ASD in particular, are likely to require increased support to move from one task to another, to complete tasks that require them to switch their focus between two competing tasks, and to locate relevant information within a busy classroom environment. As the current research has indicated, monitoring of these attentional difficulties is important as children age, with our findings supporting a trend towards more difficulties with sustained attention and overall alertness in later childhood. Whilst difficulties in these cognitive aspects of attention may also present behaviourally (e.g. child appears restless and fidgety or show poor persistence on activities), for some children
their external state may not accurately reflect their corresponding internal state of attention (e.g. while the child may be looking at the teacher or workbook, internally they may in fact be attending to unrelated inner thoughts). As such, it is imperative that parents and teachers are well informed regarding the prominence of these attentional problems in children with ASD, and that comprehensive assessment of these cognitive aspects of attention are conducted where concern is indicated (e.g. child may not present as inattentive behaviourally but is struggling to keep up in class).

Currently, psychostimulants are one of the most widely adopted treatments for attention deficits in childhood despite concerns regarding their potential impact on the developing brain; with previous research documenting potential negative side effects on appetite, sleep, growth, personality, and mood (Johnson et al., 2013; Storebø et al., 2015). Cognitive training is based on the concept that repeatedly practising a target skill will lead to improvements in that skill, as well as subsequent transfer to improvements in skills and behaviours underpinning the target skill. The feasibility of this type of training has previously been demonstrated in both TD children and in children with disorders of attention (Amso & Scerif, 2015); highlighting the possible potential of employing specific cognitive training to target those aspects of attention shown in the current thesis to be most affected in children with ASD. Employment of this kind of cognitive training for cognitive attention deficits would offer an alternative or complementary treatment approach to pharmacological and other interventions, with the potential to alleviate the deleterious impact of these attentional deficits as they emerge in early childhood.

6.4. Limitations

Whilst this thesis has led to a more comprehensive understanding of the nature of sleep and attentional difficulties in school-age children with ASD there are several limitations
which relate to the design of this study. Firstly, ASD diagnoses were not confirmed by the ‘gold-standard’ diagnostic tools; the Autism Diagnostic Observation Schedules or the Autism Diagnostic Interview – Revised. Although the potential impact of this significant limitation was minimised by obtainment and review of all children’s original paediatrician or psychologist completed diagnostic report to ensure criteria was met for a DSM-IV-TR diagnosis of autism or Asperger disorder, and through employment of the Social Responsive Scale as a screening tool, it is possible that not all participant’s in our ASD group would have met criteria on these assessment tools.

Whilst all participating children, including the ASD group, were recruited from the community, it is possible that advertisement of the research as a ‘sleep’ study may have led to an overrepresentation of sleep impaired individuals in both the TD and ASD groups due to pre-existing parental concern and subsequent interest regarding their child’s sleep. Despite this limitation, recruitment materials were consistent between groups, supporting the finding of more severe sleep problems in ASD overall.

This research is also restricted by sample size, particularly for analyses in which age-related differences were also examined. As a result, it is possible that Type II errors may have occurred. In addition, the generalisability of study findings may be limited due to homogeneity of the sample in terms of ethnicity.

The inclusion of several children in the ASD group who were taking prescription medications to aid sleep (i.e. melatonin) and behavioural symptoms of ADHD is also a potential limitation. However, given the high prevalence of both sleep difficulties and ADHD behaviours in children with ASD, it was felt that exclusion of these children would, in fact, limit the generalisability of the study findings, as well as exclude those children with significant difficulties in the areas of most interest to the study.
Finally, whilst pubertal development is known to affect both sleep and behavioural functioning, a measure of children’s pubertal stage was not included in the current study and thus its impact on both sleep and neurobehavioural functioning could not be assessed.

6.5. Directions for future research

While the current study supports that the sleep problems experienced by children with ASD are underlined by biological and behavioural factors at the very least, several pathways outlined in the model remain untested and require empirical support from future studies. Specifically, further investigation into the psychological, behavioural and social causes of sleep onset difficulties, and how these may interact with neurobiological abnormalities, as well as age-related biological changes (e.g. pubertal development), are open questions for future empirical inquiry. In addition, an exploration into the underlying mechanisms by which higher levels of hyperactivity may drive improved sleep efficiency, or vice-versa, is also interesting and requires disentangling.

Findings from Chapter 4 support a unique profile of cognitive attention difficulties in children with ASD which may serve as useful indicators by which to differentiate children with ASD from other diagnoses in which attentional dysfunction is common, such as ADHD. Future research, comparing children with ASD, both with and without a comorbid diagnoses of ADHD, to children with a diagnosis of ADHD only, on these attentional tasks would not only further increase understanding of the breakdown and development of these attentional processes within each of these disorder groups, but may also support use of these measures as tools to aid diagnosis.

Future research utilising in-home PSG may serve to further disentangle not only the nature of sleep problems in children with ASD but also the complicated relationship between sleep and attentional functioning, as highlighted by Chapter 5. The possible utility of this type
of sleep assessment in ASD is supported by a recent study by Maski and colleagues (Maski et al., 2015), and may allow analysis of different aspects of sleep microarchitecture in relationship to attention function.

Finally, in light of observed age-related changes in both attention and sleep in children with and without ASD, it is crucial that future longitudinal studies, which track children from early childhood to adolescence, are conducted in larger samples in order to increase understanding regarding the developmental trajectories of difficulties in these areas over time. This may not only have implications for the implementation of dynamic interventions over time, but also help extricate the complex relationship between children’s sleep and attention profiles.

6.6. Concluding Remarks

This body of work has added to the current evidence-base regarding attentional impairment and the nature of sleep difficulties affecting school-age children with ASD without intellectual disability, and initiated exploration of the relationship between children’s naturally occurring sleep profiles and their performance on tests of cognitive attention. Collectively, this work has highlighted prominent difficulties in objectively-measured sleep initiation, as well as dysfunction in orienting and alerting networks of cognitive attention in ASD, as well as unexpected associations between indicators of children’s sleep quality and ratings of ADHD behaviours, which appear counterintuitive and require further investigation. The early emergence of unique attentional impairments in children with ASD suggests that these deficits may represent a primary disturbance in ASD, with early intervention targeting these core deficits in attention likely to also maximise children’s learning and academic attainment. Finally, whilst the reduced sleep quality experienced by children with ASD does not appear to have direct implications for their cognitive attention function, clarification
regarding the association and direction between sleep quality and behavioural
attentionfunctioning in ASD, as well as an exploration of other psychological, biological and
behavioural factors. in association with the ASD sleep profile, has important implications for
clarification of the aetiology of sleep difficulties in this population.
References


comorbidity, and associated factors in a population-derived sample. *J Am Acad Child Adolesc Psychiatry, 47*(8), 921-929. doi:10.1097/CHI.0b013e318179964f


