Sleep and Daytime Functioning in Children on the Autism and Fetal Alcohol Spectrums

Rabya Mughal

Thesis submitted for the degree of Doctor of Philosophy

The UCL Institute of Education

Prepared under the supervision of Dr. Dagmara Dimitriou and Dr Catherine M. Hill

Acknowledgements

I would like to thank my supervisors, Dr Dagmara Dimitriou and Dr Catherine Hill for their invaluable expertise and guidance throughout this process. Dr Anna Joyce, Professor Chloe Marshall, Dr Maria Kambouri, and the members of the Lifespan Learning and Sleep Laboratory at the UCL Institute of Education have kindly contributed their valuable time and knowledge to discussing the important topics and making students feel supported, for which we are all grateful.

I would like to thank the UK FASD Alliance, in particular Maria Catterick who went above and beyond in order to facilitate this study in the hope it may help children with FASD. To Pip Williams, may she rest in peace, for welcoming me to the UK Birth Mothers Network and giving me a stark and eye-opening introduction to the complexities of this subject, which was her lifelong work.

I am indebted to the 322 children and their mums, dads, grans, foster parents, uncles and aunties who contributed to the content of this thesis in the hope that we might be able to move forward in the research on Autism and FASD.

And to my husband Samy: for all your continuous kind help, love, support, and comedy, thank you.

Impact Statement/ General Summary

Autism and Fetal Alcohol Spectrum Disorders (FASD) are neurodevelopmental conditions that affect at least 3% of the school aged population. Both have serious secondary sequelae including anxiety and depression, problems with concentration in class, learning new concepts through relevant curriculums, and social communication.

Sleep is crucial to healthy neurodevelopment. It is not just a period of rest, but a time when the brain is highly active. During sleep, the brain consolidates newly acquired information, organises memory, and can lay the basis for emotional memory. Within Autism and FASD (as well as in many other developmental and psychological conditions), sleep quality and quantity remain much lower than the average and necessary amount. It is not known why this is, but research suggests that there is a complex and bidirectional relationship between sleep and development. This relationship may be part of the compromise of atypical development.

This thesis links sleep with a number of daytime outcomes in children with Autism and FASD. According to the research carried out as part of this thesis, sleep is connected to anxiety, behaviours such as aggression and withdrawal, cognitive aspects such attention and working memory, as well as social and environmental factors. This is apparent not only in children in the neurodevelopmental categories, but in typically developing children too. This research also finds that children with Autism and FASD experience more sleep problems than typically developing children. It is therefore proposed here that sleep health interventions should be strongly considered as part of the therapeutic practice for children with Autism and FASD.

Thesis Overview

This thesis makes a novel contribution to developmental psychology by examining the associations between sleep and daytime functioning in children with Autism Spectrum Conditions (Autism, or ASC) and Fetal Alcohol Spectrum Disorders (FASD). Poor sleep is consistently noted as a secondary sequela in the developmental profiles of both Autism and FASD, and there is evidence that sleep plays a part in atypical and typical neurodevelopmental processes. Although it is not fully known, evidence suggests that causal, bidirectional relationships between sleep and neurodevelopment can explain some of the cognitive manifestations of Autism and FASD. The purpose of this thesis therefore is to examine the extent of the relationship between sleep, anxiety, executive functioning, behaviour, working memory attention, fluid intelligence and receptive vocabulary in these two neurodevelopmental conditions.

Chapter 1: This thesis begins with a literature review of the neuropsychological aspects of sleep, particularly within the context of developmental processes. There is also a focus on the developing fetus and the impact of pre and postnatal environments on later cognitive outcomes. This is followed by a review of the literature on Autism and FASD.

Chapter 2: The first study of this thesis examines the associations between sleep, anxiety, behaviour and executive functioning. Two hundred and seventy-nine caregivers completed the Children's Sleep Habits Questionnaire (CSHQ), the Behavior Rating Inventory for Executive Functioning (BRIEF), the Spence Children's Anxiety Scale (SCAS), the Child Behavior Checklist (CBCL), and a socioeconomic (SES) questionnaire. Participants were caregivers of children aged between 6-16-years with a diagnosis of FASD (*n*=114) or Autism (*n*=61). An additional sample of typically developing (TD) children were also assessed (*n*=104). Multiple regression analysis revealed that, according to parental report, sleep was a predictor of anxiety, behaviour and executive functioning in all three groups. Tests of similarity showed significantly similar behavioural and anxiety scores between children with Autism and FASD,

with both clinical groups appearing to show similar levels of panic, physical injury concerns, separation anxiety, generalised anxiety, composite anxiety scores, and levels of withdrawn behaviour. Meanwhile, executive functioning and non-adaptive behaviours were significantly different between the three groups, with several subsets scoring higher than clinical cut off points, indicating the need for clinical intervention. This statistical difference between the three groups is conceptualised within this thesis as 'syndrome specificity' and is discussed further. Chronological age, sex and SES were also predictors of sleep and daytime functioning within the statistical model.

Chapter 3: The second study of this thesis examines sleep and cognition using objective procedures: actigraphy, measuring sleep bouts and activity during the night; a Choice Reaction Time (CRT) task measuring sustained attention and inhibition; a digit span task measuring working memory; the Ravens Standard Progressive Matrices (RSPM) measuring fluid intelligence, and the British Picture Vocabulary Scale (BPVS) as a measurement of receptive vocabulary (the latter two for the purpose of understanding the child's verbal and nonverbal mental age [MA]). Participants were children aged between 6-12-years with either a diagnosis of FASD (*n*=29) or Autism (*n*=21). An additional sample of typically developing (TD) children were selected as a comparison group (*n*= 46). Group comparisons revealed that children in the clinical groups experienced shorter sleep duration and more sleep fragmentation than the TD group. Chronological age (CA), MA, sex and SES were predictors of cognitive tasks and sleep. Multiple regression analysis revealed that sleep problems were predictors of cognitive outcomes in all three groups.

Statistical comparisons between Study 1 and Study 2 showed there was a disparity between subjective and objective measurements of sleep. Whilst both methods of ascertaining sleep characteristics carry their own limitations, it was noted that such disparity may affect results and future studies on sleep in neurodevelopmental conditions should take this into account.

Chapter 4: This thesis concludes with a discussion of the role of sleep in Autism and FASD, implications of findings and areas for further investigation. Both subjective and objective measurements revealed significantly poorer sleep in the two clinical samples. Sleep disturbances as measured by caregiver questionnaire and actigraphy were significantly associated with some of the core cognitive and behavioural profiles of children with Autism and FASD. It is therefore suggested that sleep is an important target for intervention and further research is required within this field.

A note on Language

The language used in this thesis complies with the identity-first language preferred by the Autism community, and the person-first language preferred by the FASD community. Whilst the word 'condition' is preferred to 'disorder' in the Autism community, this differentiation is not prioritised in the FASD community. Within this thesis, Autism is referred to as Autism Spectrum Condition (ASC) or simply 'Autism'. Fetal Alcohol Spectrum Disorder is referred to as FASD (American Psychological Association, 2020; National Autistic Society, 2020).

The American spelling of 'Fetal' is used throughout this thesis since this is both the medical spelling of the word and the agreed spelling amongst the UK FASD research community.

List of Tables

List of Figures

List of Abbreviations

ADI-R	Autism Diagnostic Interview (Revised)
ARBD	Alcohol Related Birth Defects
ARND	Alcohol Related Neurodevelopmental Disorder
ASC	Autism Spectrum Conditions
ATP	Adenosine Triphosphate
BRIEF	Behavior Rating Inventory for Executive Functioning
CA	Chronological Age
CARS	Childhood Autism Rating Scale
CBCL	Child Behavior Checklist
CDC	Centers for Disease Control
CPAP	Continuous Positive Airway Pressure
CPT	Continuous Performance Task
CRT	Choice Reaction Time
CSHQ	Children's Sleep Habits Questionnaire
DSM-V	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
EEG	Electroencephalogram
EHCP	Education Health Care Plan
EOG	Electrooculogram
FAEE	Fatty Acid Ethyl Esters
FAS	Fetal Alcohol Syndrome
FASD	Fetal Alcohol Spectrum Disorders
fMRI	Functional Magnetic Resonance Imaging
MA	Mental Age
MEG	Magnetoencephalography
MRI	Magnetic Resonance Imaging
NREM	Non-REM
NST	Neurobehavioural Screening Tool
OSAS	Obstructive Sleep Apnoea Syndrome
PAE	Prenatal Alcohol Exposure
pFAS	Partial FAS
PLMD	Periodic Limb Movement Disorder
PSG	Polysomnography
RCPM	Raven's Coloured Progressive Matrices
REM	Rapid Eye Movement
RLS	Restless Leg Syndrome
RRBI	Restricted and Repetitive Behaviours and Interests
RSPM	Raven's Standard Progressive Matrices
SCAS	Spence Children's Anxiety Scale
SCN	Suprachiasmatic Nucleus
SDB	Sleep Disordered Breathing
SES	Socioeconomic Status
SPSS	Statistical Package for the Social Sciences
SWA	Slow Wave Activity
SWS	Slow Wave Sleep
TD	Typically Developing
ToM	Theory of Mind

Chapter 1

This chapter provides an overview of sleep and its importance to neurodevelopment, with the aim of presenting the reader with the relevant contextual evidence for this thesis. Sleep is crucial to human development, and this chapter begins with a review of the neurobiological and developmental aspects of sleep science. Within atypical populations, sleep appears to have a bidirectional relationship with the neurodevelopmental process. In the developing brain that is structurally and functionally compromised by prenatal alcohol exposure (PAE), there appear to be circadian rhythm and suprachiasmatic nuclei (SCN) anomalies which may contribute to atypical sleep patterns. In Autism, it is thought that synaptic connectivity may alter Process S, the homeostatic drive for sleep. Simultaneously, children tend to experience sleep initiation problems as a result of environmental stressors. These are additionally explained by the behavioural and affect-related profiles which are further discussed in this chapter. There remains a paucity of data in this field and Chapter 1 concludes with a short summary of the current gaps in the literature concerning sleep in Autism and FASD.

1.1 Sleep

Sleep in humans is (generally) a state of physical quiescence, identified by minimal movement, closed eyes and a characteristic body posture such as lying down or curling up. It involves reduced vigilance and responsiveness to external stimuli, until a stimulus is distinctively disturbing, or the need for sleep is exhausted. In diurnal animals, sleep starts at the onset of night when dim light cues inform the circadian rhythm to instigate a wake-sleep process and abates at the onset of morning light when that process is reversed.

This phenomenological explanation had always leant itself to the presumption that sleep was a cessation of the waking state, the purpose of which was to rest the body and mind. But in 1929 when Hans Berger decided to perform the first electroencephalography (EEG) on a sleeping person, an unusual arrangement of oscillating wave patterns was noticed that was unlike any EEG of a waking person. The first of these unusual oscillations, which were named the Berger (or alpha, α) wave, appeared during 'quiet wakefulness', a period during which the participant was conscious but with closed eyes. On opening his eyes, the α waves would stop. The longer and deeper the participant slept, the more concentrated the EEG activity would become (Berger, 1929). In 1937, Loomis, Harvey & Hobart found further oscillating EEG patterns occurring at different stages of the night. They divided these findings into five distinct stages of sleep marked by the frequency and amplitude of the observed EEG patterns. Today these are consolidated into three stages, rather than five, and contribute to the current classification of Non Rapid Eye Movement (NREM) sleep (Loomis, Harvey, & Hobart, 1937). In 1953 Eugene Aserinsky and Nathaniel Kleitman introduced the electrooculogram (EOG) alongside the EEG to assess eye movements during sleep. The resulting discovery was Rapid Eye Movement (REM) sleep, approximately twenty-minute periods of quick, binocular, random eye movement, characterised by mixed frequency, low voltage EEG patterns, and often accompanied by dreaming. These periods of REM were noted to have occurred several times a night with a mean interval of 2

hours 16 minutes (Aserinsky & Kleitman, 1953). Three stages of NREM and one period of REM make up one sleep cycle lasting around ninety minutes in adults. The architecture of sleep changes throughout the lifespan and adult sleep generally involves five full cycles a night.

In addition to these early experiments were others exploring the neuroanatomical areas involved in sleep. The treatment of soldiers who had sustained injuries during war led to two discoveries: those who had wounds in the lower brain stem area were paralysed but had intact sleep and wake cycles, whilst those who had wounds in the upper brain stem area were more likely to be in a permanent coma (Espie & Morin, 2012). It was thus was proposed that the superior (topmost) area of the brain stem was involved in the activation of the sleep/ wake process. Moruzzi and Magoun (1949) discovered through electrical stimulation of various subcortical areas that the upper brain stem was involved in the activation of the synchronised and desynchronised patterns observed in Loomis et al.'s EEG recordings. They proposed that the reticular formation of the brain stem was responsible for maintaining a state of wake in the cerebral cortex, and named this region the reticular activating system (Moruzzi & Magoun, 1949). In contrast, Walter Hess (1951) discovered that an area of the thalamus, when electrically stimulated in cats, induced sleep onset and a synchronised EEG pattern characteristic of NREM and identical to spontaneously sleeping cats. This area was named the hypnogogic zone (Hess, Akert & Koella, 1951). Put together, these early experiments laid the foundation for the current knowledge of the physiology of sleep architecture.

1.1.1 Sleep architecture

The typical conscious and unconscious state is comprised of six separate categories marked by alpha, beta, theta, delta, Slow Wave Activity (SWA) and REM activity. EEG recordings gather patterns of electrical-chemical activity in the brain through the measurement of action potentials, which are created when large populations of neurons simultaneously release or inhibit neurochemicals. This leaves either a positive or negative charge in the neuron, depending on the direction of travel or

neurochemical involved (Kahn, Dan, Groswasser, Franco, & Sottiaux, 1996). High amplitude waves during sleep indicate that large groups of neurons are simultaneously coordinating or communicating across the cerebral cortex, measured in Hertz (Hz), or number of waves/ cycles per second. This culminates in SWA: the slow, high amplitude and synchronised waves of the third NREM stage (see Figure 1.1). EEG measures fluctuations of voltage between groups of neurons in various cortical and subcortical areas. These are comprised of a series of sine waves which can be 'de-composed' through Fourier Analysis, the mathematical measurement of the frequency, amplitude, and 'power' of the EEG recording per second. This is knowns as Delta Power and is used as a measurement of the intensity of sleep (Kropotov, 2009).

The six separate categories of wake and sleep can be viewed in Figure 1.1 and are categorised as the following:

i. **Wakefulness**, a state of full consciousness where interaction with the environment can occur. During wake, EEG patterns are characterised by desynchronised, rapid, waves of high frequency and low amplitude, in the beta (β) range, of 14-40Hz. This is accompanied by high muscular tone in EMG recordings.

ii. In **relaxed wakefulness**, or pre-sleep state, Berger (or alpha, α) waves of 8-12Hz are observed. These are waves of lower frequency and higher amplitude than β, indicating an increase in the synchrony of neural activity.

iii. **NREM stage 1** (N1). Typically, NREM stages are characterised by decreased muscle tone, regular respiration and a gradual slowing of EEG frequency into increasingly synchronised, low frequency waves in the theta (θ) range of 4-8Hz. Spectral analysis additionally shows that subcortical regions (not always visually apparent in EEG) display a background pattern of slow wave activity (SWA) which may have important functional implications. N1 is a period of decreased wake or drowsiness where individuals start failing to respond to auditory stimuli,

however arousal thresholds are low and when woken up in this stage an individual may report of having not been asleep at all. EOG recordings in this phase indicate slow but randomly directed eye movements.

iv. **NREM stage 2**, or light NREM sleep (N2). During N2, eye movements cease, the heart rate slows down and the body temperature decreases. This process allows the body to prepare to enter deep sleep. Background oscillations decrease to slow, 5Hz in the delta (δ) range. Punctuated within this are two types of periodically superimposed events: sleep spindles which last between 0.3 – 5 seconds, in the sigma (σ) range of 11-16Hz; and K complexes which are characterised by a negative sharp wave of high amplitude immediately followed by a positive neighbour with a total duration of around 0.5 seconds. K complexes are mostly recorded in frontal electrodes.

v. **NREM Stage 3**, N3, or slow wave sleep (SWS). N3 is the deepest stage of NREM sleep and is characterised by the slowest waves in the delta or 0.5-2Hz range. Similar to K complexes, slow waves are usually detected at the frontal electrodes. At N3 arousal thresholds are usually high and waking from this stage of sleep involves a longer period of sleep inertia, and possible confusion or disorientation at waking. N3 sleep may also involve slow, pendular eye movements which indicate the onset of REM sleep.

vi. **REM sleep**. Unlike NREM, REM is characterised by desynchronised, rapid, low-amplitude EEG activity that resembles wakefulness and low amplitude mixed frequency in the 15-30Hz range. It is also characterised by irregular, sharp eye movements, muscular atonia and cardiovascular and breathing irregularities. Phasic twitches can also be detected by EMG during REM sleep. K-complexes or sleep spindles appear during REM, usually in the first REM of the night cycle.

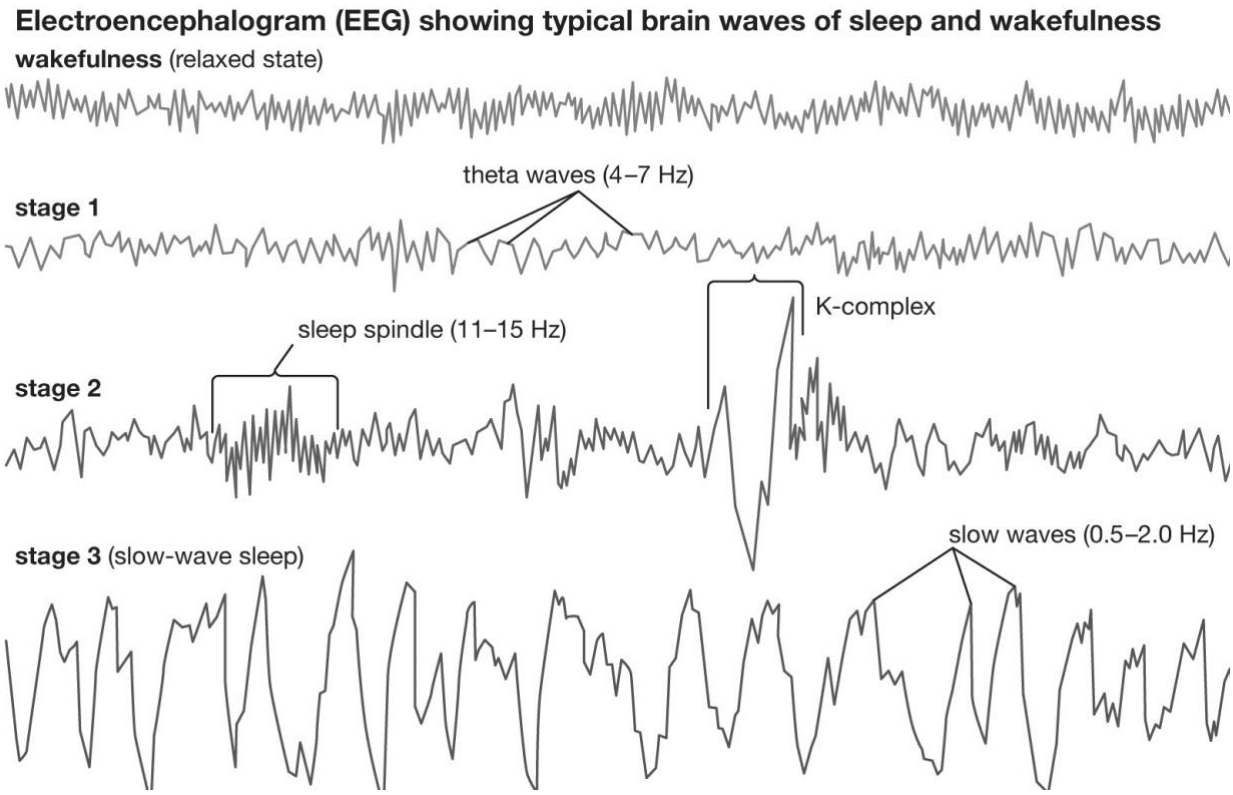


Figure 1.1: EEG of Sleep and Wake: the Oxford Handbook of Sleep Disorders (2013)

An adult sleep cycle consists of the three phases of NREM and REM (In order: N1, N2,N3,N2,N1,REM). Generally, each night consists of five cycles, however the length of each phase differs through the night. The first REM of the night is shorter, usually lasting around 10 minutes. The second REM lasts longer than the first, around 20-30 minutes, and the third to fifth will last upwards of 45 minutes and dominate later cycles. It is not yet fully known why the length of REM sleep increases as the night progresses (Espie & Morin, 2012).

1.1.2 Sleep and development

What eventually becomes adult sleep architecture develops through a series of incremental changes corresponding with the major milestones of human development, starting prenatally and continuing throughout the lifespan.

1.1.2.1 Sleep in utero and at birth

Sleep-wake rhythms develop prenatally. Before birth, the human fetus demonstrates four distinct behavioural states that reflect fetal nervous system activity. These behavioural states parallel the sleep–wake stages of infants and children, and are classified using fetal heart patterns, body movements, and eye movements into 4 states: quiet sleep (analogous to NREM), active sleep (analogous to REM), quiet wake, and active wake (Nijhuis, Prechtl, Martin, & Bots, 1982). This rest-wake activity may be dependent on maternal sleep-wake states (Blumberg, Gall, & Todd, 2014; Micheli et al., 2011). Ultrasound visualisations show movements, such as stretching and spontaneous limb movements, from around 10 weeks' gestation (Hoppenbrouwers et al., 1978). At around 30 weeks' gestation, periods of quiescent movements called fetal-rest-activity patterns occur around 50% of the time, increasing to 60% nearer to full term, and indicate a prenatal distinction between sleep and wake (DiPietro, 2016; Hoppenbrouwers & Sterman, 1975).

1.1.2.2 Sleep in new-borns -12 months

New-born infant sleep is distributed throughout the day and night and lasts around 16-17 hours per 24 hours, decreasing to 14-15 hours by 16 weeks of age, and 13-14 by 6 months of age (Davis, Parker, & Montgomery, 2004). New-born sleep follows an ultradian rhythm of around 4 hours, which appears to be based around the feeding cycle (Espie & Morin, 2012). At around four months the organisation of REM and NREM sleep is apparent, with sleep cycles lasting between 30-70 minutes and gradually increasing throughout development. Sixty percent of 6-month-old and 80% of 9-month-old infants sleep throughout the night, as the circadian sleep-wake pattern is established. During the day, wakefulness increases while daytime sleeping becomes consolidated into regular naps. Daytime sleep tends to occur during three to five naps at 6 months old and around two naps at 9-12 months, and is comprised of more stage 1 and 2 sleep than stage 3 and REM sleep (Mindell & Owens, 2015).

1.1.2.3 Sleep in early childhood (1-5 years)

Sleep cycles and REM sleep begin to organise in early childhood. Sleep onset latency (the amount of time to fall asleep) averages around 15-30 minutes at this age and the transition from NREM to REM on average takes around 15 minutes (Kahn et al., 1996). At sleep onset, NREM dominates the early child sleep cycle. Between the ages of 1-5 years REM sleep decreases from 30% to the adult 20-25%. Sleep cycles are approximately 40 minutes long at around 2 years and gradually increase in length to 60 minutes at 5 years of age. At this point, children have around 7-10 cycles during each nocturnal sleep period (Kahn et al., 1996). During early childhood, daytime napping decreases and night sleep typically becomes consolidated into periods of 10 hours. As children become more socially aware, cognisant, imaginative and verbal, they are more likely to demonstrate a desire to prolong bedtimes, request parental attention or have nightmares and night wakings (Meltzer & Mindell, 2006).

1.1.2.4 Sleep in mid childhood (6-10 years)

Throughout mid-childhood total sleep time decreases but remains around 2-3 hours longer than adult sleep time. By the age of 10 years children should be sleeping around 8-10 hours a night and sleeping for around 95% of that time (Mindell & Owens, 2015). During middle childhood, parasomnias such as enuresis, sleep talking, sleep walking, or night fears are seen in up to 30% of typically developing (TD) children (Mindell & Owens, 2015).

In recent years it has been established that children in mid childhood are the most alert of any age group, have the longest sleep latencies and tend to not fall asleep during multiple sleep latency tests (MSLTs, tests using EEG to assess sleep latency, consisting of five naps across a full day, based on the assumption that the quicker an individual falls asleep the more sleep deprived they are) or have sleep onset latency of <8 minutes in the absence of hypersomnia (Littner et al., 2003). This is thought to be due to the dysrhythmia of the suprachiasmatic nucleus (SCN), two clusters of neurons (nuclei) within

the hypothalamus, directly above the optic chiasm which are responsible for the process of circadian rhythm functioning (Fernandez et al., 2014).

1.1.2.5 Sleep in adolescence (11-18 years)

As they mature, adolescents generally tend to show a reduction in maintaining adequate sleep, but no reduction in the need for sleep. This can result in a decrease in total sleep time and an accumulation of sleep debt. When Arora and colleagues (2013) measured sleep and correlates in adolescent children (*n*=632) they found older adolescents had shorter sleep times than younger adolescents (15-18 years = 7.79 ± 1.17 hours; 11-14 years = 8.76 ± 1.35 hours) (Arora et al., 2013). The recommended amount of sleep for children aged 6-13 years is 9-11 hours, and for teenagers aged 14-17 years 8-10 hours (National Sleep Foundation, 2016).

A number of psychosocial factors have been found to affect sleep patterns during this phase of development, particularly as children transition into adolescence and enter a period of increased independence and responsibility. During this time, parental control tends to decrease, and a number of developmental milestones are reached, such as the freedom to choose bedtime and morning routines, increased social independence and usage of online media (Carskadon & Dement, 2011). Early school starts can deprive adolescents of sufficient sleep, particularly in instances where academic pressures increase. In one study by Lo, Lee, Lee, Sasmita, Chee et al (2018), school starting times were delayed for 45 minutes for a sample of 12-16-year-old adolescents in Singapore (*n*=375). Wellbeing measures taken by the Positive and Negative Affect Schedule (Watson, Clark, & Tellegen, 1988) after one month and nine months of delayed school start times, and actigraphy was used to measure sleep times. At both measurement time points, participants reported fewer sleep problems, lower depression scores, and lower negative mood scores (Lo et al., 2018).

Polysomnography (PSG) in adolescence shows a decrease in SWS in a linear fashion throughout puberty stages with an approximate 35% decrease from Tanner stage 1 to 5 (Sarchiapone et al., 2014). At this point, the percentages of REM and NREM appear to reach adult levels, with REM periods increasing in length as the sleep period progresses. Daytime alertness tends to decline as adolescents grow and mean sleep-onset latency falls in mid-adolescence. MLST studies show shorter sleep onset latency after mid puberty (Tanner stage 3; mean age 13.4 years) and then remain at a reduced level (Sarchiapone et al., 2014). Daytime sleepiness is also apparent in this population where older adolescents tend to report greater difficulty with daytime sleepiness and nocturnal sleep than younger adolescents. Daytime sleepiness tends to occur mainly in the mid-afternoon (Carskadon & Dement, 2011) but this time is not confined to adolescence: hence the development of the biphasic 'siesta' in various cultures.

1.1.3 Process S and Process C

The need for sleep is driven by two processes that occur in tandem. Process S and Process C are influential in the effort to reach sleep when it is needed and timely. These processes are also mediators in cognitive outcomes in individuals, as will be discussed in Chapter 3 of this thesis.

1.1.3.1 Sleep homeostasis, or "Process S"

Sleep is not an optional behaviour, but a state-regulated response to sleep-wake history (Krause et al., 2017). The homeostatic drive for sleep is directed in part by the decrease in energy reserves in the brain. Unlike other cells in the body that can metabolise amino and fatty acids in the restoration of cells, the brain is sustained only by glucose in the form of astrocytic glycogen in the blood, or glial cells. Adenosine triphosphate (ATP) is a complex nucleoside with many biochemical functions, including protein synthesis and the transfer of energy between cells, DNA transcription, and neurotransmission. It is also involved in the initiation of sleep and wake. The brain becomes energy

compromised when glycogen is depleted, which causes the release of astrocytic glycogen from glial cells. This activates ATP and induces the sleeping process. A greater sleep need after a period of sleep deprivation results in greater Delta Power (see Section 1.1.1). Delta Power can therefore be used to extrapolate sleep intensity, as well as sleep deprivation. In instances of sleep deprivation Delta Power is greater at sleep onset but declines to its regular rate afterwards. This indicates that there is a high need for sleep at the beginning which slowly declines as sleep continues throughout the night. Wake is triggered in part by the repletion of energy to the brain and the process repeats itself throughout the day (Krause et al., 2017). This is known as Process S.

1.1.3.2 Circadian rhythm or "Process C"

Biological outcomes taken from light and dark cues are endogenous to all living things and are known as circadian rhythms (Carskadon & Dement, 2011). In humans, circadian rhythms are entrained by light. Time giving (zeitgeber) cues at appropriate times in the phase response curve (PRC) prevent free running of the circadian rhythm. The PRC can be advanced or delayed if zeitgeber cues are not timely, for example in the case of jet lag or night shift working. When light cues enter the retina, they are processed in the hypothalamus, and are organised in the SCN. This pathway is known as the retino-hypothalamic tract. The SCN is the area of the brain that controls the circadian rhythm, and when given zeitgeber cues it sends messages to various other regions, including: the preoptic area which (along with the reticular activating system and lateral hypothalamus) controls arousal, sleep and their transition; the dorsomedial nucleus of the hypothalamus, which regulates wakefulness via the modulation of the neurotransmitters hypocretin and orexin; regions such as the paraventricular hypothalamic nucleus, which manages the release of sleep-wake modulating chemicals such as melatonin and cortisol. Advances or delays in the PRC can result in conditions such as Advanced or Delayed Sleep Phase Syndrome, or Seasonal Affective Disorder (Meerlo, Mistlberger, Jacobs, Craig Heller, & McGinty, 2009).

On a cellular and molecular level, the circadian system is comprised of a self-sustaining oscillation, an input system, and an output system. The oscillation mechanism is comprised of a gene translation-transcription system, which provides feedback for the oscillation. Waking light cues set the mechanism for the translation-transcription of several genes that are involved in the circadian process: PER (period); TIM (time); CLOCK (circadian); CRY and CYCLE (sensitive to blue light) and BMAL1 (turns on the expression od PER and CLOCK). Dark cues output Gamma Aminobutyric Acid (GABA), an inhibitory neurotransmitter which sets off the neurochemical process of sleep through the inhibition of wake neurotransmitters, releasing melatonin, and so sleep follows (Meerlo et al., 2009).

The neurobehavioural responses to the homeostatic drive for sleep are phenotypic, and may involve genetic components including circadian genes (Goel, Basner, Rao, & Dinges, 2013). So, both Process S and Process C work in synchrony with each other, in a symbiotic fashion, as can be seen in figure 2.

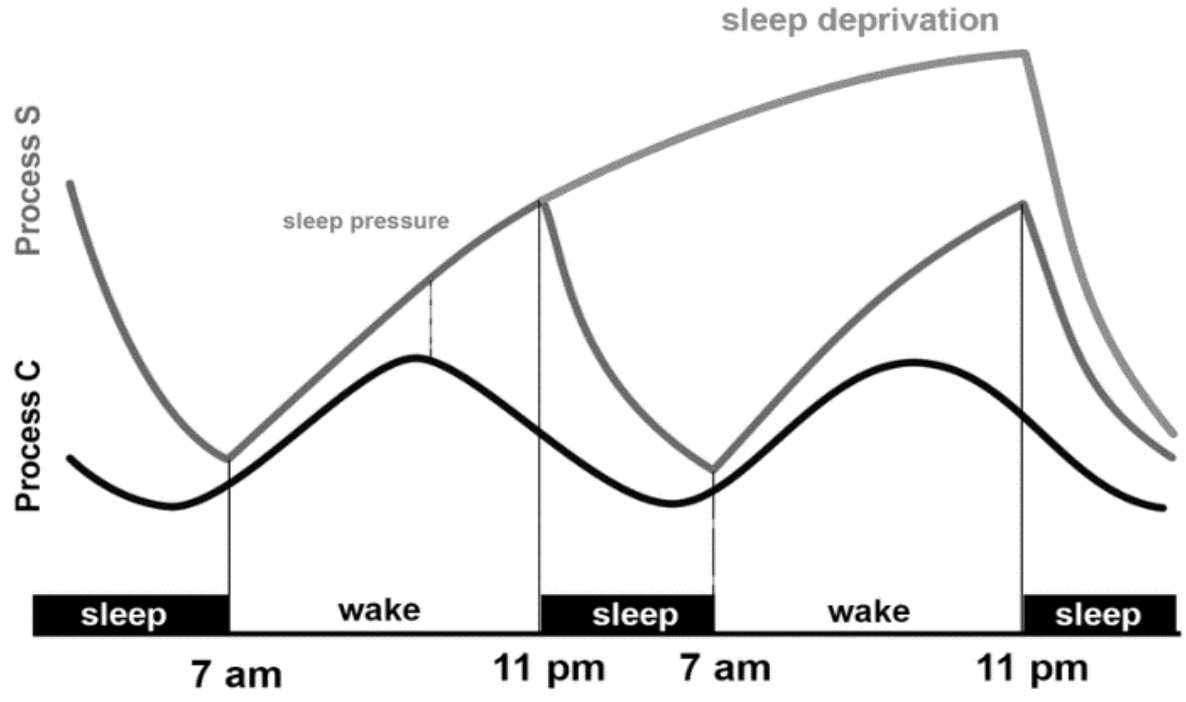


Figure 1.2: Visual model of Process S and Process C: The Oxford Handbook of Sleep and Sleep Disorders (2013)

Much of what is known about sleep has been gained through the study of its associations with daily functioning and memory consolidation. Many aspects of psychological and physiological functioning in some way incur a penalty as a result of sleep deprivation (Frank & Heller, 2003). Total sleep deprivation eventually results in psychosis, multi organ failure, dementia and death (Tabernero et al., 2000). Yet, there is currently no full consensus on the functions of different sleep stages, although mounting evidence suggests one vital role is the consolidation of newly experienced information and their stabilisation into long term memory. In the next section, a broad overview will be given about (some of) the functions of sleep. In the following chapters, which explore the relationships between sleep and daytime functioning in two clinical populations, further sleep functions pertaining to the studies will be outlined.

1.1.3.3 Sleep and physiology

Whilst it is beyond the scope of this thesis to give a comprehensive overview of this subject, it is important to point to the existence of the vast body of literature that exists on the physiological functions of sleep. Sufficient sleep is associated with lower risks of cardio-metabolic disease, respiratory disorders, epilepsy, inflammatory disease, chronic pain, and obesity and diabetes due to its role in metabolic processes. Consequently, epidemiological studies indicate that sufficient sleep duration is associated with lower mortality rates (Cappuccio, Miller, Lockley, & Rajaratnam, 2018). Much like its counterpart, wakefulness, the functions that are served by the process of sleep fall into several different domains within the cognitive and physiological sphere.

1.1.3.4 REM and NREM and daytime functioning

Sleep is fundamental to the developmental process and plays a role in cognition, neuroplasticity, brain maturation and optimal daytime functioning. Neuronal processes occurring at the cellular level during NREM and REM underlie a number of local and global organisational tasks and processes, including

memory consolidation, task learning, and the formation of neural pathways organising visual, auditory, and integrated or abstract events (e.g. Carskadon & Dement, 2011; Espie & Morin, 2012; Frank & Heller, 2003; Hill, Hogan, & Karmiloff-Smith, 2007; Meltzer & Mindell, 2006).

Sleep deprivation produces an increase in daytime sleepiness, and a decrease in sleep onset. After prolonged periods of sleep deprivation, the duration of NREM N2 can shorten to minutes or seconds, and the duration of N3, SWS and REM increases (Carskadon & Dement, 2011). This increase in REM is known as REM Rebound and is experienced in sleep deprived individuals, including sleep apnoea patients after the introduction of continuous positive airway pressure (CPAP; Frank, 2018). The decrease in NREM and increase in REM duration has a number of implications around the function and timing of NREM and REM. Firstly, a longer period of REM after sleep deprivation indicates that one of its functions is a restorative one. This is also supported by the fact that glial cells facilitate the depletion of astrocytic glycogen during wakefulness and replete it during sleep (Bellesi et al., 2018; Frank 2018). Secondly, since it is always necessary for NREM to occur before REM, it can be suggested that there is a homeostatic relationship between these two sleep stages, or that NREM contains a trigger mechanism for REM and vice versa (Frank & Heller, 2003). In fact, REM manipulation studies indicate that one of the functions of REM is to enhance SWA in subsequent NREM cycles (Kashiwagi & Hayashi, 2016). Therefore, REM and NREM seem to proceed in congruence with each other.

A growing body of literature suggests that NREM and REM sleep are part of a homeostatic system that is responsible for normal intellectual function and behaviour. Sleep Onset REM (SOREM) occurs in situations of total sleep deprivation (Frank & Heller, 2003). EEG recordings show that individuals, when sleep deprived for long periods of time, can experience 'microsleeps' or can show NREM activity whilst awake. Prolonged deprivation of REM sleep results in a decrease of physiological function, behaviour change including aggression, a decrease in the delta power of NREM, and fragmented sleep over the night (Goldschmied, 2018). However, as noted above, such studies contain methodological limitations

and it is difficult to extrapolate the function of REM as a process in and of itself through depriving it in humans. NREM is instigated by various cortical and subcortical regions, including the thalamus for bioelectrical events, and the basal forebrain and posterior regions such as the cerebellum, caudal stem, hypothalamus and spinal cord for homeostatic regulation. NREM seems to be a necessary function allowing synaptic connections to normalise back to a basal level, ensuring cellular homeostasis (de Andrés, Garzón, & Reinoso-Suárez, 2011), whilst simultaneously (or perhaps after) consolidating memory (Cappuccio et al., 2018).

1.1.3.5 Sleep and memory

A considerable amount of the neurophysiological research theorising the mechanistic process (and function) of sleep focusses on how different sleep stages facilitate memory consolidation, and over the past several years an interesting association between sleep and memory has been discovered. Memory is a vast psychological concept made up of a number of components and mechanisms to which this thesis cannot do justice, suffice to say it includes short term, long term, sensory, procedural, declarative or topographic memory, and in some form or another each is called upon for the efficient functioning of higher order processes. Newly formed long-term memory is consolidated through a process of stabilisation in which newly learnt information is encoded following an initial experience from an environmental stimulus, while neurophysiological responses store information until it is retrieved through a process of reactivation (Khonsary, 2017). Initially this information is fragile and can be interrupted by a number of behavioural, pharmacological or neurochemical interferences, but over periods of time the memory becomes resilient to interference through the process of consolidation (Alberini & Ledoux, 2013). It is now known that sleep plays a role in building the neural pathways required for memory consolidation, however this does not appear to be a completely linear process. Different types of memory consolidation may be dependent on different stages of sleep (Goel, Rao, Durmer, & Dinges, 2009). Research conducted in adult populations suggests that when

sleep occurs after episodic-emotional, declarative and procedural memories, and those associated with reward gain, such memories are enhanced to a greater extent than without sleep (Diekelmann, Wilhelm, & Born, 2009). Slow wave sleep enhances declarative memories through a process of activation and reactivation, which can be observed in PSG through hippocampal-neocortical SWA. Recent studies suggest that this can occur both spontaneously and can be externally triggered, for example through odour cueing, the process of reintroducing odours that form part of a learning task during sleep (Klinzing et al., 2018; Klinzing, Rasch, Born, & Diekelmann, 2016). Meanwhile, studies suggest that NREM and REM provide different functions for the process of memory consolidation. In a series of studies conducted by Gais and Born (2004), REM sleep appeared to support procedural and emotional memory consolidation, whilst slow wave sleep was more associated with declarative memory consolidation (Gais & Born, 2004). Newer studies suggest that REM may be required for spatial and contextual memory consolidation. In one rodent study conducted by Boyce, Williams and Adamantidis (2017), a group of rodents were subject to REM sleep suppression by suppressing GABA, an inhibitory neurotransmitter involved in the onset of REM. This resulted in normal fear-conditioned memory recall, but impaired spatial object and contextual memory recall (Boyce, Williams, & Adamantidis, 2017).

However both REM and NREM can also overlap in their roles in procedural, declarative and episodic memory, and further studies suggest that sleep spindles also contribute to the causal mechanism of memory consolidation (Klinzing et al., 2018). In an experiment using a computerised task that required complex motor and working memory training (finger tapping task) using the participant's non dominant hand, Huber and colleagues (2004) found EEG recordings that night showed higher levels of SWA and spindles in the motor cortex cortical/ subcortical areas that controlled the hand that was newly trained (Huber, Ghilardi, Massimini, & Tononi, 2004). Similarly, EEG recordings show that cortical and subcortical area SWA related sleep spindles correspond to motor and sequence learning (Barakat et al., 2011).

Sleep and memory consolidation is an area of interest to those wishing to understand the typical and atypical developing brain. TD children learn at a fast pace during development, particularly when they are school aged, and frequently, actively and quickly consolidate novel material – a process that requires successions of consolidation of arbitrarily related information. During development, SWA and the ability to form episodic memories are established during infancy and increase during childhood (Huber & Born, 2014). Periods of sleep shortly after exposure to new information can improve declarative memory in children (Ashworth et al., 2014), and sleep promotes word learning in children who read story books at bedtime (Williams & Horst, 2014). In understanding the neural mechanisms of sleep dependent learning in children, Urbain et al. (2016) conducted magnetoencephalography (MEG) on a sample of school aged (*m*=10.0 years) children (*n*=21) during a picture identification task in which 100 coloured outline drawings of unfamiliar non-objects were associated with 'magic' properties. Children were then divided into two groups, one of which napped for 2 hours while the other spent time in quiet wakefulness. Those who spent time in SWS were significantly more likely to have learnt a higher number of 'magical' properties of non-objects (Urbain et al., 2016).

Taken together, both paediatric studies and those conducted with adults reveal that longer periods of sleep are associated with better memory (Tucker, Humiston, Summer, & Wamsley, 2020). However, this appears to be dependent on sleep architecture. This thesis (and many studies assessing the association between sleep and cognition) relies on the assumption that more sleep facilitates better cognition, however, to be more precise, better quality sleep and full sleep cycles are more likely to facilitate cognitive outcomes. This is apparent in paediatric clinical populations, where sleep and declarative memory is variable and may be vulnerable to differences in neurodevelopmental profile. In a cross-syndrome comparison study conducted by Ashworth, Hill, Karmiloff-Smith and Dimitriou (2017), a sleep dependent declarative memory task was administered to groups of school aged children with Down Syndrome (*n*=20), Williams Syndrome (*n*=22), and TD children (*n*=33) in which novel non-word animal names were learnt and retested after intervals of wake and sleep. Whilst the

task performance of TD children improved after a period of sleep, children with Down Syndrome tended to improve after a period of non-sleep, whilst children with Williams Syndrome tended to improve both with and without sleep. This suggests time-dependent, rather than sleep-dependent learning in these populations (Ashworth, Hill, Karmiloff-Smith, & Dimitriou, 2017). Similarly, sleep-dependent declarative memory was examined by Fletcher and colleagues (2019) in a sample of school aged children with Autism and TD aged matched controls (*n*=54). Non-word animal names were learnt and retested the following day and one month later, and PSG was measured in both groups. Children with Autism showed significantly less NREM and fewer sleep spindles than TD children. Sleep spindles were associated with learning new semantic knowledge, whilst in the Autism group, sleep spindles were significantly associated with improvements in familiar names, although this may be a reflection of consolidating priorities in the Autism group rather than a reflection of the role of NREM in new semantic knowledge in this population (Fletcher et al., 2019).

1.1.4 Sleep disorders in typical development

Between 10-30% of TD children experience sleep disturbances during childhood, although only around 4-10% are diagnosed with sleep disorders, classified by the International classification of Sleep Disorders (Greydanus, 2018; Meltzer & Mindell, 2006). Up to 70% of children and adolescents in the UK have inadequate sleep (Kelly, Zilanawala, Booker, & Sacker, 2018). Sleep disorders are categorised into: insomnias, sleep related breathing disorders, central disorders of hypersomnolence, circadian rhythm sleep-wake disorders, parasomnias, sleep-related movement disorders and other sleep disorders. Some of the more common childhood sleep disorders are outlined below.

1.1.4.1 Childhood insomnias

Insomnia is defined as the persistent inability to initiate or maintain sleep, despite adequate opportunity and circumstances to do so, lasting a period of three months or more, that have daytime

consequences. Behavioural insomnia is the most common childhood sleep problem and typically presents as bedtime resistance, prolonged sleep onset and night wakings (Mindell, Boyle, Butler, Lipari, & Meltzer, 2014).

Behavioural Insomnia related to sleep onset is characterised by prolonged night waking that results in insufficient sleep, which may have resulted from negative or habitual sleep associations. For example, if the child has learnt to only fall asleep under certain conditions (rocking, parent in the room, special toy, bedtime story), they will require these conditions when aroused at the end of each sleep cycle and will not be able to self soothe until the same conditions are made available (Mindell & Owens, 2015).

Behavioural Insomnia related to parental limit setting refers to children's oppositional behaviour at bedtime. This can include bedtime resistance, verbal protests or 'curtain calls', such as getting out of bed to ask a question, go to the toilet one more time, have one more story, etc. Bedtime stalling (without psychopathological reasons) can result from a number of factors, such as an intrinsic circadian preference of night time, not understanding the concept of bedtime, or zeitgeber cues from screen lights that delay the phase response curve (see Section 1.1.3.2).

Psychophysiologic insomnia, or conditioned insomnia, refers to sleep onset delay or poor sleep maintenance that is caused by heightened physiologic or emotional arousal related to sleep and the sleep environment. In younger children with active imaginations this may result from fears such as monsters, zombies, witches etc. whilst in older children and adolescents this could result from fears around school, academic performance, friendship problems or other ruminations of anxiety. Persistent ruminations are associated with a higher incidence of nightmares which can exacerbate the symptoms of conditioned insomnia (Meltzer & McLaughlin Crabtree, 2015).

1.1.4.2 Sleep-disordered breathing

Sleep-disordered breathing (SDB, an obstruction of the airway which can hinder the attainment of full sleep cycles) can manifest in a continuum of conditions that range in severity, from snoring and upper airway resistance to obstructive sleep apnoea syndrome (OSAS) with secondary sequelae such as growth impairment, neurocognitive or cardiovascular problems resulting from systemic inflammation and oxidative stress (Dehlink, 2016). It is thought that around 10-14% of children under the age of 6, 11% of children aged 4-11, and 6% of adolescents snore (Young, Peppard, & Gottlieb, 2002). Due to increased muscle atonia, SDB occurs more during REM sleep. Risk factors increasing the likelihood of SDB include enlarged tonsils or adenoids, obesity, craniofacial anomalies and muscle weakness (Gokdemir & Ersu, 2016). Recent data also show that the rise in obesity amongst children has resulted in the increase of OSA in children, which is associated in turn with increased cardiovascular burden and metabolic syndromes (Glaser & Styne, 2017).

1.1.4.2.1 Parasomnia

Parasomnias are non-deliberate motor or subjective phenomena occurring during the transition between different sleep states. These can include abnormal movements or behaviour that are the result of central nervous system activity, and in the International Classification of Sleep Disorders – third edition (ICSD-III) are categorised into NREM-related, REM-related parasomnias, sleep related movement disorders, and other parasomnias.

NREM parasomnias in children include disorders of arousal, such as sleep walking, night terrors and confusional arousals. These occur more commonly in the first half of the night. REM parasomnias include nightmares, nightmare disorder, sleep paralysis or REM Behaviour Disorder (RBD) and tend to occur later in the night. Other parasomnias that are not confined to a specific sleep state include sleep

related hallucinations, enuresis or unspecified, medication related, or parasomnia related to a co-occurring condition (Espie & Morin, 2012).

Parasomnias are common in early to mid-childhood due to the developing central nervous system and are usually outgrown in adulthood. Familial history of parasomnias and psychiatric diagnoses increase the likelihood of parasomnias. Parasomnias are more likely to occur in children with early life trauma or experiencing emotional distress and are experienced by between 5-11% of the paediatric population (Agargun, Boysan, & Hanoglu, 2004;BMJ 2020).

1.1.4.3 Sleep Related Movement Disorders (SRMD)

As opposed to parasomnias, SRMDs are a group of simple, monophasic movement disorders that can disturb sleep. The ICSD-III classifies these as restless leg syndrome (RLS), periodic limb movement disorder (PLMD), bruxism, myoclonus at sleep onset and myoclonus of infancy, rhythmic movement disorder, sleep related leg cramps, as well as SRMDs due to medical disorders, medication or substance, or unspecified SRMD.

PLMD is characterised by involuntary, repetitive and highly stereotyped limb movements whilst asleep, occurring 20-40 seconds apart and common to N2 sleep. It is identified through the periodic movement of limbs sleep index (PMLSI) score of 5 or more and is associated with disturbed sleep and excessive daytime sleepiness. PLMD is characterised by dorsiflexion of the toes and ankles and occasional flexion of the hip and knee. It occurs in around 10% of children and prevalence is thought to increase with age, with a prevalence of up to 34% of individuals over 60 (Frye et al., 2017). There is an increased incidence of PLMD in children with Attention Deficit Hyperactivity Disorder (ADHD). RLS, a condition characterised by the strong urge to move one's legs, and PMLD seem to be associated with ADHD (Walters, Silvestri, Zucconi, Chandrashekariah, & Konofal, 2008).

1.1.5 Sleep and atypical populations

Although heterogenous, those in atypical populations experience higher rates of sleep disturbances than neurotypical individuals. One meta-analysis conducted by Surtees and colleagues (2018) revealed that those with an intellectual disability (defined as an IQ <70) slept for an average 18 minutes less than the typical controls in their respective studies. Whilst there may have been selection bias and inaccuracies due to poor measurement or methodology, 93% of those with intellectual disabilities experienced poorer sleep (Surtees, Oliver, Jones, Evans, & Richards, 2018). Given its importance to memory, cognition and neurodevelopment, it seems reasonable to assume that sleep plays a significant part the everyday life of an individual with a neurodevelopmental condition, neurocognitive condition or condition of affect. Although the causative reasons for sleep problems in atypical populations are yet only theorised, there is strong evidence that the developmental process is bidirectional and reliant on the function of sleep (Surtees et al., 2018).

Syndrome specific behavioural and architectural sleep problems have been identified in Angelman, Cri du Chat and Cornelia de Lange Syndrome (Tietze et al., 2012), Down Syndrome and William Syndrome (Ashworth, Hill, Karmiloff-Smith, & Dimitriou, 2017; Horne, Wijayaratne, Nixon, & Walter, 2019) Fragile X Syndrome (Kronk et al., 2010),Prader Willi Syndrome (Cotton & Richdale, 2006), Smith Magenis Syndrome (Tietze et al., 2012) as well as idiopathic conditions resulting in intellectual disability, among others (Esbensen & Schwichtenberg, 2016). Sleep problems are also higher in neurodevelopmental conditions such as Autism (Mannion & Leader, 2014), ADHD (Spruyt & Gozal, 2011b), Fetal Alcohol Spectrum Disorders (Chen, Olson, Picciano, Starr, & Owens, 2012; Inkelis & Thomas, 2018), in conditions relating to affect and disinhibition such as Schizophrenia (Kaskie, Graziano, & Ferrarelli, 2017), Depressive, Dissociative and Bipolar Disorders (Gold & Sylvia, 2016), Anxiety and Obsessive Compulsive Disorders (Chase & Pincus, 2011), as well as later developing neurocognitive conditions such as Dementia (Elwood et al., 2011) and Parkinson's Disease (Chaudhuri

et al., 2002). Sleep problems in these atypical populations impact negatively on daytime functioning, affect, as well as have an impact on caregivers, whose own sleep may be disturbed due to nocturnal demands (Esbensen & Schwichtenberg, 2016). Early identification and intervention in sleep disorders is an increasingly important area of therapeutic concern, especially given that sleep interventions can have the ability to ameliorate behavioural symptoms. To give an example, individuals with ADHD who present with sleep problems miss more days from school, show intensity in symptomology, and appear to have a lower quality of life (Spruyt & Gozal, 2011b). Paediatric studies have found that SDB is associated with difficulties in behavioural and emotional regulation, school performance, sustained attention, selective attention and alertness (Beebe, 2011; Sung, Hiscock, & Sciberras, 2008; Young et al., 2002). Surgical treatments (tonsillectomy) in children with ADHD and SDB have shown improvements in behavioural symptomology (Fidan & Fidan, 2008).

Further research would benefit this area. For example, there is a need for more meta-analytical data assessing sleep patterns in individuals with atypical prefrontal functioning (social disorders), such as Autism, ADHD, disorders of conduct, FASD, major depressive disorders and those around disinhibition, compulsivity or phobia. Such an analysis might find, as Esbesen (2017) and Surtees (2018) found in intellectual disabilities, that several sleep problems cluster around certain syndromes. This may also be the case with conditions which rely on social awareness and understanding.

1.1.6 How is sleep measured?

Whilst PSG is considered the 'gold standard' of sleep measurement due to its comprehensive analysis of the sleeping body, there are several limitations to its use in infants, children, and those with neurodevelopmental conditions. Well controlled laboratory settings include: continuous observations by a clinician; scalp EEG and EOG recordings; EMG placed on the chin; ECG to measure cardiac events; oral and/or nasal airflow measures with thermistors and pressure measures along with measures of O_2 and CO_2; an actigram to measure body movement; pulse oximetry, amongst other measurements

depending on the sleep clinic. Whilst methodologically sound, such studies often have different outcomes to the less intrusive environments an infant or child's home. The phenomenon of the 'first night' effect may additionally question the reliability of PSG results, in which adaptation to new equipment or environment may cause disruption to an individual's normal sleep habits. This is particularly relevant in clinical populations where sensory issues or a change in environment may cause distress to a child (Espie & Morin, 2012).

Furthermore, individual variations in the development of the circadian rhythm in the infant mean that differences in the timing of observations yield varying results. Studies taken during night sleep differ from day sleep, for example morning naps tend to be more dominated by REM sleep than afternoon naps, and night time sleep in infants shows varying lengths of REM and NREM sleep (known as active and quiet sleep in infants). Much of this literature is based on the observation of the breathing and movement of the sleeping infant (Kahn et al., 1996).

Sleep measurements relevant to this thesis are outlined below.

1.1.6.1.1 Actigraphy

Actigraphy measures epochs of gross motor activity to infer sleep and wake parameters, based on the procedure of recording and integrating the frequency and degree of movement over time. It is usually worn as a watch like device on the non-dominant wrist for a minimum period of one week, depending on the clinical practice. Algorithms are applied to the epoch data to estimate whether an individual is asleep or awake, which in turn generate a number of sleep parameters (see Table 1.1). In a systematic review and meta-analysis conducted by Smith and colleagues (2018), 81 studies using actigraphy were assessed for their efficacy in evaluating sleep disorders, and the use of actigraphy relative to sleep logs and PSG. When compared to sleep logs, actigraphy yielded significantly different results in the area of sleep duration, with mean differences of 37.4 minutes, whilst there was more variability with

PSG in sleep duration, with significant and non-significant differences (4.6 minutes – 83.4 minutes difference). Wake After Sleep Onset (WASO) was more similar in PSG, actigraphy and sleep logs with no significant differences or distinct information. Depending on the studies assessed, sleep efficiency was either in agreement between actigraphy and PSG (2.1% difference in sleep efficiency between actigraphy and PSG), or provided significantly different results (8.1% difference in sleep efficiency between actigraphy and PSG). Depending on the devices used, the nature of the participant and validity of data, PSG may yield similar results to actigraphy (Smith et al., 2018).

There are some limitations to the use of actigraphy to objectively measure sleep. Like PSG, participants may experience a 'first night effect' in which the appearance of a device measuring sleep may alter an individual's behaviour. Additionally, there may be an inaccuracy in the assumption that motion detection is a measurement of sleep; this is an issue in individuals with compromised mobility. Whilst actigraphy is well validated for the estimation of sleep parameters within school aged children, its estimation for sleep onset latency and daytime sleep is less reliable, perhaps because of its reliance on accurate caregiver reports on 'lights out' times (Martin & Hakim, 2011).

Whilst PSG yields more in-depth data on an individual's sleep architecture, actigraphy is a non-intrusive device that can comfortably be worn at home, is a commonly used measurement of sleep in children, and is particularly useful for clinical populations for whom sleeping in a different environment away from home is difficult. An overview of the actigraphy parameters measured as part of this thesis are outlined in Table

Table 1.1: Actigraphy Parameters

Actual sleep time	Total time spent in sleep according to epoch-by-epoch category
Actual sleep (%)	Expressed as a percentage of assumed sleep time
Actual wake time	Total time spent in wake according to epoch-by epoch
Actual wake (%)	Actual wake time expressed as a percentage of the assumed sleep time.
Sleep efficiency (%)	Actual sleep time expressed as a percentage of time in bed.
Sleep latency	Time between "Lights Out" and "Fell Asleep".
Sleep bouts	Number of contiguous sections categorised as sleep in the epoch-by-epoch wake/sleep categorisation.
Wake bouts	Number of contiguous sections categorised as wake in the epoch-by-epoch wake/sleep categorisation.
Mean sleep bout	Average length of each sleep bout
Mean wake bout	Average length of each wake bout
Immobile mins	Total time categorised as Immobile in the epoch-by-epoch mobile/immobile categorisation.
Immobile time (%)	Mobile time expressed as a percentage of the assumed sleep time.
Mobile mins	Total time categorised as mobile in the epoch-by-epoch mobile/immobile categorisation.
Mobile time (%)	Mobile time expressed as a percentage of the assumed sleep time.
Immobile bouts	Number of contiguous sections categorised as immobile in the epoch-by-epoch mobile/immobile categorisation.
Mean immobile bout	Average length of each of the immobile bouts.
Immobile bouts <=1min	Number of immobile bouts which were less than or equal to one minute in length.
Immobile bouts <=1min (%)	Number of immobile bouts less than or equal to one minute expressed as a percentage of the total number of immobile bouts.
Total activity score	Total of all the activity counts during the assumed sleep period.
Mean activity /epoch	Total activity score divided by the number of epochs in the assumed sleep period. Note that this result will be expected to scale depending on the length of the epoch.
Mean nonzero activity epoch	Total activity score divided by the number of epochs with greater than zero activity in the assumed sleep period. Note that this result will be expected to scale depending on the length of the epoch.
Fragmentation Index	Sum of the "Mobile time (%)" and the "Immobile bouts <=1min (%)". This is an indication of the degree of fragmentation of the sleep period and can be used as an indication of sleep quality (or the lack of it).

1.1.6.2 Questionnaires

Whilst objective measurements of sleep provide more clinically accurate measurements of sleep patterns, caregiver questionnaires are often used as an easier, more cost-effective method of evaluating children's sleep.

In a systematic review of instruments used for the measurement of sleep in paediatric populations, Spruyt and Gozal (2011a) evaluated 57 questionnaires for content, validity and reliability. Psychometric instruments of sleep were theorised as showing: 1. Purpose; 2. Research Question; 3. Response Format; 4. Generation of Items; 5. Pilot; 6. Item-analyses and non-response analyses; 7. Structure; 8. Reliability; 9. Validity; 10. Confirmatory analyses; and 11. Standardisation and norms development. Out of the 57 instruments picked up by the review criteria, two met all eleven quality criteria – the Sleep disturbance scale for children (SDSC) and the Sleep Disorders Inventory for Students (SDIS) (Spruyt & Gozal, 2011a). For the purposes of this thesis, neither were used. The SDIS, whilst robust, was not freely available, and the SDSC, whilst it fulfilled the 11 items mentioned above, was a 26 item test assessing sleep initiation, SDB, arousal, sleep-wake transition, excessive somnolence which it was felt would not cover the social aspects of sleep behaviour (such as sleep anxiety and bedtime resistance) that are experienced by children with conditions of social conduct pertinent to this thesis. Moreover, it was felt that because the few previous studies assessing FASD used the Children's Sleep Habits Questionnaire (CSHQ), replication of these studies using the same instrument would give further validation to the studies presented within this thesis.

The CSHQ is a 33-item caregiver report covering major clinical presentations of childhood sleep problems (Owens, Spirito, & McGuinn, 2000). It is a popular instrument used in previous similar research in neurodevelopmental conditions. It covers the quality criteria 1,2,3,5,8, and 9 formulated by Spruyt and Gozal (2011a) mentioned above but most notably it misses 4. Generation of items; 6. Item-analyses and non-response analyses; 7. Structure; 10. Confirmatory analyses; and 11. Standardisation and norms development. Most notably this instrument does not have confirmatory analysis, which will be discussed in Study 1 of this thesis, in which the CSHQ is used as a measure of sleep, and in Study 2 of this thesis, in which objective and subjective sleep measurements are compared. The CSHQ measures sleep 'habits', entrenched behaviours around sleeping that may contribute to disordered sleep, and also measures some sleep problems, which are problems around

the physiological process of sleep. These are: Bedtime resistance (behavioural; refusing the bedtime routine, stalling bedtimes, engaging in 'curtain calls' – asking for one more drink, one more story); Sleep Onset Delay (behavioural/ physiological; problems with normal transition from waking to sleep states); Sleep Duration: (behavioural/ physiological; sleeping the right amount); Sleep Anxiety (perceptual/emotional, leading to behavioural; feeling anxious about sleeping due to preconceived fears of night time, being away from a parent, etc); Night Waking (behavioural/ physiological: arousals at the end of sleep cycles with the inability to fall back asleep without the original conditions attached to falling asleep); Parasomnia (physiological, underpinned by perceptual/emotional, may result in behavioural: nightmares, night terrors, sleep walking, talking in sleep. The CSHQ also includes bruxism, excessive movement and enuresis which although aren't technically classified as Parasomnias in the ICSD-III); SDB (physiological; measured in the CSHQ through asking whether the child snores, snorts, gasps or breathes loudly during sleep); Daytime Sleepiness (behavioural leading to physiological: whether the child falls asleep during relaxed or playful activities during the day as a result of sleep debt). The use of the CSHQ was important in this thesis given that it enabled previous studies to be replicated, however its limitations do mean that standardised results are not yielded, and it has not been validated in clinical populations.

When measuring paediatric sleep, there tend to be inconsistencies between caregiver report and objective measurements, particularly if the caregiver is unaware of night wakings or that particular sleep behaviours are unusual or not age appropriate (Meltzer & Mindell, 2006). Parental questionnaires used in conjunction with objective measurements can gain a richer picture of a child's sleep pattern. As it is noted later in this thesis, such discrepancies may lead to conflicting results.

1.1.7 Summary

The reduction in consciousness during sleep is an evolutionary enigma which suggests that sleep must have a vital function if it renders an organism vulnerable to predators. It must be the case that the processes that are performed during sleep are not possible whilst conscious or cannot be carried out 'in the background' of an otherwise conscious brain.

EEG recordings show that a pattern of low frequency waves dominate sleep, during which time it Is theorised that the sleeping brain is consolidating memory. The specific functions of NREM and REM in cognition are not yet fully known but mounting evidence points towards their role in procedural and declarative memory. In particular, sleep spindles and SWA are thought to contribute to memory consolidation, and by extension, task performance. The existence of a cycle between NREM and REM suggests an interactive process, in which one benefits the other until the function is exhausted. This is supported by evidence that information between cortical and subcortical areas is reversed during NREM and REM and suggests an ongoing dialogue throughout the night. This is an important facilitator of cognitive processes since memory, in its various forms, is always called upon for cognitive tasks, as well as behavioural, social and emotional processes. Sleep need increases with prior wakefulness, and more so after daytime learning. There is a considerable amount of literature examining the causal, correlational and bidirectional associations between sleep and neurocognitive function which suggest that sleep plays a vital role in cognitive processes. Moreover, sleep plays an important part in human development and follows certain patterns as children and adolescents mature. It is vital to the neurodevelopmental process given its relationship to memory processing and cognition. Sleep is compromised in atypical populations and there is a paucity of data in this newly emerging area.

When measuring sleep, objective and subjective methodology is useful; there are strengths and limitations to both. In paediatric clinical populations where objective sleep data is required, PSG is methodologically robust but may yield inaccurate results due to 'first night effects', or may yield no

results at all in populations where change in environment or sensory load may impact participation. Meanwhile actigraphy is a less invasive method of sleep measurement, however results may not capture true sleep problems due to methodological and validation constraints. Caregiver reports reveal accurate subjective data on perceived sleep problems, however may not be accurate at yielding clinical information. A combination of objective and subjective reports may provide a better overview of an individual's sleep parameters.

In the following sections, two neurodevelopmental conditions are outlined in which sleep problems are often highlighted by caregivers. Research suggests that sleep is highly associated with cognitive outcomes not only in these two conditions but in numerous atypical populations in which development is compromised, as well as in the typically developing population.

1.2 Fetal Alcohol Spectrum Disorders (FASD)

Ethanol is a teratogen which passes freely through the umbilical artery into the placenta and amniotic fluid, where it remains equal to maternal levels after it has been expelled from the maternal system. The human placenta has minimal capacity for metabolising alcohol and does not identify it as a waste product. It is instead turned into fatty acid-ethyl esters (FAEE) and remains in the fetal compartment for a prolonged period (Burd, 2007). Simultaneously, the fetal liver is unable to metabolise or remove ethanol, FAEE or acetaldehyde (a by-product of metabolised ethanol). Low levels of alcohol cause umbilical cord spasm and vasoconstriction, affecting fetal growth, placental development and cellular function (Burd, Roberts, Olson, & Odendaal, 2007). Consistent levels of alcohol consumption during pregnancy results in the disruption of fetal growth and contribute to a spectrum of physiological and neurodevelopmental issues, the resulting arrangement of which is known as Fetal Alcohol Spectrum Disorders (FASD).

The consequences of prenatal alcohol exposure (PAE) were first described by Lemoine (1968), Ulleland (1972), Jones and Smith (1973a;1973b), who recorded patterns noted in infants born to women with alcohol addiction: small head circumference; low birth weight-height ratio; craniofacial characteristics (small eye openings, palpebral fissures, smooth vermillion and philtrum); structural complications to the renal, respiratory, cardiovascular and visual systems, and neurodevelopmental delay. It is the latter 1973 paper by Jones and Smith which is credited with the discovery of Fetal Alcohol Syndrome (FAS), named as such in the hope it would deter future pregnant women from drinking (Jones et al., 1973). However, since its discovery, the incidence of FASD has increased exponentially and the effects of PAE are now considered far more subtle and endemic than originally described. The type and extent of fetal growth disruption depends on the amount, timing and frequency of PAE, and can be affected by other factors such as additional teratogens (e.g. cocaine, cannabis or heroin) which can exacerbate the effects of alcohol on fetal development. The timing and dosage of alcohol in pregnancy has an

impact on fetal outcomes, but not in a linear fashion. Risk factors that can exacerbate the development of FASD additionally include maternal nutrition and metabolism, epigenetics and other yet unknown fetal vulnerability factors (Mukherjee, 2014).

1.2.1 Diagnostic criteria

FASD occurs along a spectrum, with FAS considered the most 'severe' since the majority of individuals with FAS have low but functional IQ, while individuals with FASD can have variable IQ and cognitive profiles, including typical or low IQ (Kodituwakku, 2009). Other conditions in the spectrum include: Partial Fetal Alcohol Syndrome (pFAS), Alcohol-Related Neurodevelopmental Disorder (ARND), and Alcohol Related Birth Defects (ARBD). FAS is identified by craniofacial characteristics, whilst the presentation of psychological or physiological presentations constitute the diagnostic criteria of the other conditions. Whilst the identification of FAS is more straightforward, diagnostic categories for ARND, ARBD and pFAS vary from country to country and there remain some differences in terminology and diagnostic criteria (see Table 1.2).

Uncertainty around prenatal conditions, such as the social stigma of admitting to drinking during pregnancy, and the high number of children with FASD in the care of adults other than the birth mother, mean that the first diagnostic category of FASD (confirmed prenatal alcohol exposure) is often not ascertainable (Mukherjee, 2019). Caregivers other than the birth parents might suspect prenatal alcohol exposure to be the cause of their child's difficulties but cannot confirm it. For this reason, it is thought that a high proportion of children and adults with FASD remain undiagnosed (Morleo et al., 2011).

A neurodevelopmental profile of FASD is not yet clear, although a pattern of cognitive and behavioural functions is anecdotally reported (Williams, Catterick, & Calder, 2012). It is not always possible to confidently discriminate between individuals with PAE and a pathognomonic neurodevelopmental

pathway, and individuals without PAE but with a similar neurodevelopmental pathway, partly because the effect of PAE is highly variable and dependent on environmental and genetic factors (Kodituwakku, 2009; Lange, Rovet, Rehm, & Popova, 2017). Thus, the diagnostic description of FASD remains excluded from the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V). Neurodevelopmental Disorder Associated with Prenatal Alcohol Exposure (ND-PAE) which appears in the DSM-V appendix is used as a diagnostic term, but an increasing number of paediatricians use the term FASD as a diagnosis (Mukherjee, 2019). The International Classification of Diseases, tenth edition (ICD-10) lists FAS under the Q86 Code 'Fetal Alcohol Syndrome (dysmorphic)', and whilst other conditions on the FASD spectrum are not included, they can be included under the Q35 code 'Maternal care for suspected damage to fetus from alcohol' or Q86 code 'Congenital malformation syndromes due to known exogenous causes, not elsewhere classified'.

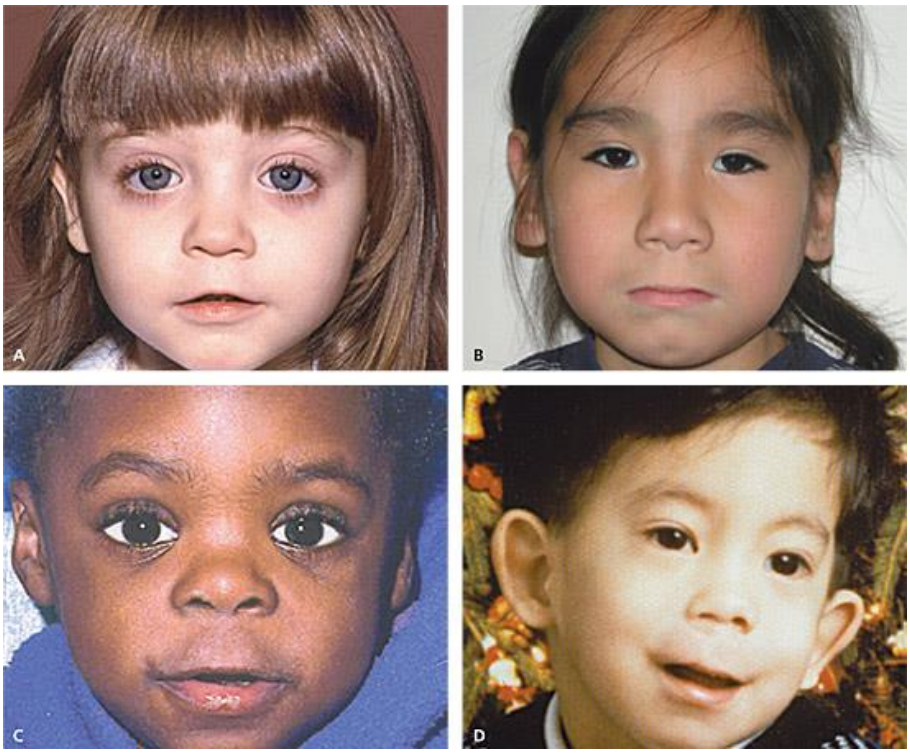


Figure 1.3: Craniofacial characteristics of FAS in different ethnic populations: Microcephaly (small head size); palpebral fissure (extended distance between the eyes); smooth philtrum (cleft); thin upper lip; low nasal bridge. Used with permission from the UK FASD Alliance.

Table.1.2: Diagnostic Criteria for FASD

	Institute of Medicine (Hoyme et al., 2016)	**FASD 4-Digit Code (Astley, 2013)**	**Centers for Disease Control** (CDC Centers for Disease Control, 2005)	**Canadian Guidelines (Cook et al., 2016)**
Fetal Alcohol Syndrome (FAS)	*(Requires all 4 criteria)* 1. Confirmed or unconfirmed maternal alcohol exposure 2. Facial features – evidence of a characteristic pattern of facial anomalies that includes features such as short palpebral fissures and anomalies in the premaxillary zone (e.g., flat upper lip, flattened philtrum, and flat midface). 3. Growth retardation – at least one of the following: - Low birth weight for gestational age - Decelerating weight over time not due to nutrition - Disproportional low weight to height. 4. CNS neurodevelopmental abnormalities. At least one of the following: - Decreased cranial size at birth - Structural brain anomalies - Neurological hard or soft signs (age appropriate).	*(Requires all 4 criteria)* 1. Confirmed or unconfirmed maternal alcohol exposure 2. Facial Features: all 3 from Washington FAS Guide: - Philtrum Rank 4 from the guide - Upper lip rank 4 or 5 - Palpebral fissure length <3rd percentile. 3. Growth retardation: antenatal or postnatal height or weight ≤10th percentile. 4. CNS – at least one of: - Structural evidence of CNS damage (e.g., head circumference <3rd percentile, significant brain abnormalities on neuroimaging) - Neurological evidence of CNS damage - Significant impairment across 3 or more domains of brain function (generally ≤2 standard deviations). Domains include executive function, memory, cognition, social/adaptive skills, academic achievement, language, motor, attention, and activity level.	*(Requires all 4 criteria)* 1. Confirmed or unconfirmed maternal alcohol exposure 2. Simultaneous presentation of short palpebral fissures (≤10th percentile), thin vermillion border, smooth philtrum (ranks 4 and 5) 3. Height or weight ≤10th percentile at any point in time. 4. Head circumference ≤10th percentile or structural brain abnormality or neurological problems or other soft neurological signs outside normal limits or functional impairment as evidenced by global cognitive or intellectual deficits, below the 3rd percentile (2 SD) below the mean or functional deficits below the 16th percentile (1 SD) below the mean in at least 3 domains:	*(Requires all 4 criteria)* 1. Confirmed or unconfirmed maternal alcohol exposure 2. Facial features – all 3 of: Philtrum rank 4 or 5, Upper lip rank 4 or 5, Palpebral fissure length ≤3rd percentile. 3. Growth retardation – at least one of: Birth weight or birth length ≤10th percentile for gestational age; Height or weight ≤10th percentile; Disproportionately low weight-to-height ratio (≤10th percentile). 4. CNS – evidence of impairment in 3 or more of the following CNS domains with impairment indicated by function ≥2 standard deviations from the mean: Hard or soft neurological signs; Brain structure; Cognition; Communication; Academic achievement; Memory; Executive functioning and abstract reasoning; Attention deficit/hyperactivity; Adaptive behaviour; Social skills; Social communication.

Table 1.2 continued: Diagnostic Criteria for FASD

	Institute of Medicine (Hoyme et al., 2016)	**FASD 4-Digit Code (Astley, 2013)**	**Centers for Disease Control** (CDC Centers for Disease Control, 2005)	**Canadian Guidelines (Cook et al., 2016)**
Partial FAS (pFAS)	*(diagnosis requires sections 1 and 2, and one other):* 1. Confirmed maternal alcohol exposure. 2. Facial features – evidence of some components of the pattern of characteristic facial anomalies. 3. Growth retardation. At least one of the following: - Low birth weight for gestational age - Decelerating weight over time, not due to nutrition - Disproportional low weight to height 4. CNS Neurodevelopmental abnormalities. At least one of the following: Decreased cranial size at birth; Structural brain anomalies; Neurological hard or soft signs (age appropriate): Evidence of a complex pattern of behaviour or cognitive abnormalities that are inconsistent with developmental level and cannot be explained by familial background or environment alone, such as learning difficulties; deficits in higher-level receptive and expressive language; poor capacity for abstraction or metacognition; specific deficits in mathematical skills; or problems in memory, attention, or judgement.	*(diagnosis requires sections 1, 2 and 3):* 1. Confirmed maternal alcohol exposure. 2. Facial features – at least 2 of: - Philtrum rank 4 or 5 - Upper lip rank 4 or 5 - Palpebral fissure length <3rd percentile. 3. CNS – at least one of: - Structural evidence of CNS damage (e.g., head circumference <3rd percentile, significant brain abnormalities on neuroimaging) - Neurological evidence of CNS damage - Significant impairment across 3 or more domains of brain function (generally ≤2 standard deviations). Domains include executive function, memory, cognition, social/adaptive skills, academic achievement, language, motor, attention, and activity level.	Not Proposed N/A – Felt that there was insufficient data to provide guidance for this diagnosis. Formed group to discuss	*Requires all 3 criteria:* 1. Confirmed maternal fetal alcohol exposure. 2. Facial features – 2 or more of: - Philtrum rank 4 or 5 - Upper lip rank 4 or 5 - Palpebral fissure length <3rd percentile. 3. CNS – evidence of impairment in 3 or more of the following CNS domains with impairment indicated by function ≥2 standard deviations from the mean: Hard or soft neurological signs; Brain structure; Cognition; Communication; Academic achievement; Memory; Executive functioning and abstract reasoning; Attention deficit/hyperactivity; Adaptive behaviour; Social skills; Social communication.

Table 1.2 continued: Diagnostic Criteria for FASD

	Institute of Medicine (Hoyme et al., 2016)	**FASD 4-Digit Code (Astley, 2013)**	**Centers for Disease Control** (CDC Centers for Disease Control, 2005)	**Canadian Guidelines (Cook et al., 2016)**
Alcohol Related Neuro Develop-mental Disorder (ARND)	(*Diagnosis requires Section 1 and one other)* 1. Confirmed maternal alcohol exposure. 2. CNS neurodevelopmental abnormalities – any of the following: - Decreased cranial size at birth - Structural brain anomalies - Neurological hard or soft signs (age appropriate) 3. Evidence of a complex pattern of behaviour or cognitive abnormalities that are inconsistent with developmental level and cannot be explained by familial background or environment alone, such as learning difficulties; deficits in higher-level receptive and expressive language; poor capacity for abstraction or metacognition; specific deficits in mathematical skills; or problems in memory, attention, or judgement.	ARND or ARBD: - The 4-digit code uses different categories and terminology to describe children with neurodevelopmental problems, some of which may be comparable with ARND.	Not Proposed N/A – Felt that there was insufficient data to provide guidance for this diagnosis. Formed group to discuss	*Requires both criteria:* 1. Confirmed maternal alcohol exposure. 2. CNS – evidence of impairment in 3 or more of the following CNS domains: CNS – evidence of impairment in 3 or more of the following CNS domains with impairment indicated by function ≥2 standard deviations from the mean: Hard or soft neurological signs; Brain structure; Cognition; Communication; Academic achievement; Memory; Executive functioning and abstract reasoning; Attention deficit/hyperactivity; Adaptive behaviour; Social skills; Social communication.
Alcohol Related Birth Defects (ARBD)	(*Diagnosis requires Section 1 and one other)* 1. Confirmed maternal alcohol exposure, and one or more birth defects: - Cardiac anomalies - Skeletal anomalies - Renal anomalies - Ocular anomalies - Auditory anomalies	ARND or ARBD: - The 4-digit code uses different categories and terminology to describe children with neurodevelopmental problems, some of which may be comparable with ARND.	Not Proposed N/A – Felt that there was insufficient data to provide guidance for this diagnosis. Formed group to discuss	Not Proposed

At present, no single neuropsychological test has both sensitivity and specificity to work as a diagnostic evaluation tool for ARND and diagnostic procedures vary from country to country (Lange et al., 2017). In the UK, after prenatal alcohol exposure has been confirmed (or is suspected), strong risk factors (gestation <37 weeks, higher parity/ gravidity, and higher birth order of child) and weak risk factors (Alcohol Dehydrogenase AD1B1/B3 genotype, maternal tobacco use, decreased maternal weight, child height and head circumference, increased maternal age) are assessed (BMJ Best Practice, 2020a). Consequently, a battery of psychometric tests is administered (measuring executive functioning, visual motor integration, receptive and expressive vocabulary, psychiatric screening, cognition, behaviour – parental and teacher report, memory and attention). In the UK, children's FASD diagnoses are made with the combined effort of a clinical psychologist (to ascertain psychometric measures), paediatrician (for craniofacial, CNS, growth diagnostics and/or high/ low risk factors) geneticist (to test for AD1B1/B3 genotype), as well as social workers, birth family where this is possible, teachers and foster or adoptive caregivers (to contribute to the evidence of PAE and behavioural profile). Whilst full FAS can be diagnosed by a paediatrician and geneticist, the diagnosis of ARND when the facial features are not present is less straightforward. A combination of observation, medical history and screening tests must exclude any other conditions before a diagnosis of ARND can be made. The behavioural characteristics of FASD overlap with a number of other conditions, with Conduct Disorder being its most prevalent neurological co-occurrence (Mukherjee, 2019). Others are ADHD, Oppositional Defiant Disorder (ODD), Autism Spectrum Condition (ASC), or wider neurodevelopmental presentations such as Tourette's Syndrome. Confidently diagnosing FASD involves differential diagnostic practices to exclude the common co-occurrences (Morleo et al., 2011).

1.2.2 Neurodevelopmental profile

The widespread neural damage incurred by PAE means children with FASD may have difficulties with a number of physical and neurocognitive functions. These are often compounded by the environmental stressors that are also common to the psychosocial environment of the child with FASD, which are additionally taken into account. The primary aetiology of FASD is alcohol consumption, which is variable, whilst pathological features include maternal and fetal high/low risk factors (BMJ Best Practice, 2017). Therefore, the extent of the presentation of neurodevelopmental features varies in each child. Nonetheless, a pattern of behaviour is generally observed by clinicians, education professionals and caregivers which is collated below.

Neonatal indications of FASD include a combination of growth, craniofacial, musculoskeletal, urogenital (including renal), cardiac, hearing and visual anomalies (Brown, 2013). Infants malnourished in the womb usually emerge ravenous and eager to feed, whilst in infants with FASD, problems with latching on to the nipple and decreased muscle tone lead to feeding difficulties and frequent hospital referrals as a result of poor weight gain (Brown, 2013). As a consequence, neonates with FASD tend to present with weight, length and head circumferences in the lower quartile. In children with FASD, adequate nutrition may restore the child to a typical weight and height, however children with FAS usually remain within the lower weight and height quartile despite adequate nutrition. Diagnostic craniofacial features of FAS are small head circumference, alongside syndromic philtrum, palpebral and nasal bridge features. Aside from these, infants may present with prognathism, cleft palate or posterior rotation of the ears (BMJ Best Practice, 2020a). Anecdotal evidence from caregivers suggests that in early infancy erratic sleep cycles may appear with no predictable sleep wake pattern (Brown, Freeman, Pickett, Watts, & Trnka, 2018).

Toddlers with FASD tend to show little interest in food and are slow to gain weight. Developmental milestones are generally reached at this age, but the gap between the toddler with FASD and the TD toddler may begin to appear (Catterick & Curran, 2014). Toddlers with FASD can be prosocial, indiscriminate with social contact and friendships, excessively talkative, or may display short attention spans, distractibility and hyperactivity. They may have an inability to comprehend verbal warnings and danger and may have increased temper tantrums and show non-compliance. They tend to show a preference for routines and 'sameness', however this may be an age where the changing of foster carers and disruptions to routines may be more noticeable (Price, Cook, Norgate, & Mukherjee, 2017).

During school age, children with FASD develop a pattern of social, emotional and behavioural characteristics, but these can be highly variable. Some children may show high levels of prosocial behaviour and no conduct disorder, whilst some might show proficiency in certain cognitive tasks but present with high levels of internalised behaviours such as anxiety (Brown & Mather, 2016). During the first two years of school, reading and writing milestones generally tend to be reached whilst mathematical concepts tend to be more difficult to understand (Glass, Ware, & Mattson, 2014). The hippocampal vulnerability to prenatal alcohol exposure results in problems with learning, memory and verbal skills (Willoughby, Sheard, Nash, & Rovet, 2008). The majority of children with FASD function with IQs within a low, but standard (i.e. 75-85) range. Children with FAS, however, tend to have more severe symptomology, such as significantly lower IQ, on average between 65-75, and tend to fall within the limited intellectual functioning range (Mattson, Crocker, & Nguyen, 2011). Heavy prenatal alcohol exposure has a stronger relationship with lower cognitive scores (Alati et al., 2006), particularly in the memory and verbal domain, during the first trimester (Willford, Leech, & Day, 2006). Children with FASD may appear to be verbose but recall ability on verbal information is lower than in TD populations (Willford et al., 2006). This means that whilst children may appear to know many words, they may not understand their meanings.

School aged children with FASD can present with poor fine and gross motor skills and appear

uncoordinated and clumsy, or have problems with handwriting, fastening buttons and zips or doing up shoelaces. This can be seen in the skills profile developed by Lucas, Latimer, Doney, Watkins, Tsang et al. (2016), who compared fine manual control and manual coordination in a sample of 7-9 year old children with FASD (*n*=108) in comparison toa control TD group. In this study, rates of fine manual control and manual coordination were within the average to low range, and significantly lower than TD controls (Lucas et al., 2016).

Impulsivity, emotion and behaviour in children with FASD is also substantially documented. This is because areas such as inhibition, impulsivity, control, aggression and emotional regulation are more often externalised than internalised and present as the more concerning areas for caregivers. Children with FASD are likely to present with challenging behaviours that often reach clinical thresholds (Glass et al., 2014). Children may display attentional problems around vigilance, reaction time, and the speed or inhibition of information processing (Lange et al., 2017). In fact, around 60% of children with FASD also fall into the diagnostic category of ADHD, both of which are characterised by patterns of inattentiveness, hyperactivity and impulsiveness (Coriale et al., 2013). However, children with FASD are more likely to have different patterns of neuronal pathology that result in the attentional symptoms of ADHD, so interventions that are designed for children with ADHD do not have the same effect on children with FASD (Kodituwakku, 2009). For example, whilst individuals with idiopathic ADHD may be able to recognise the impact of their behaviour, children with FASD tend to not make the same link between cause and consequence. This means that reward based interventions and social stories that are often used for children with ADHD are not as effective (Gautam et al., 2015). Additionally, adverse social experiences intensify the coping patterns of children with FASD (Novick Brown, Connor, & Adler, 2012). Conduct disorder, which presents with patterns of antisocial, aggressive, destructive and deceitful behaviour, is the most prevalent psychiatric comorbidity to FASD, and in FAS is present in 90.5% of the population, in comparison to around 9% of the general population (Popova, Lange, Shield, et al., 2016). In one clinical study of 547 children with FASD referred to a FASD

clinic in Chicago, 42% had a diagnosis of ADHD, while 68% had diagnoses of internalising disorders related to emotion or affect including anxiety, psychosis and bipolar disorder (Chasnoff, Wells, & King, 2015). Caregiver psychopathology can additionally impact child development. Maternal depression is more likely to result in internalising behavioural comorbidities in FASD, whereas PAE without maternal psychopathology is related to externalising behaviours (Mattson et al., 2011).

Hyper and hyposensitivity also feature heavily in the daily functioning of a child with FASD. Children may show externalising, irritable or aggressive behaviours in some environments but can also appear to be friendly, calm and talkative in others. This can be confusing for caregivers when the difference between the two environments is not apparent. Often, a modification of the sensory environment can minimise the effects of over stimulation or sensory overload. Children with FASD can be hypersensitive to sudden or persistent noises, or to loud sounds, music, loud voices and other sounds that may not be noticed by others. This also extends to certain visual or physical sensory inputs resulting in unusual behaviours or the inability to cope (Jan et al., 2010).

Children with FASD tend to show problems in adaptive behaviour such as social functioning, communication, and levels of daily function (e.g. personal hygiene, getting dressed, using the appropriate language with peers, or efficiently managing free time). Compared to typically developing children, those with FASD show difficulties in identifying emotion, nonverbal cues, facial expressions and tone of voice (Lange et al., 2017). This may include difficulty in understanding humour or irony, expressions in social interactions or distinguishing reality from fiction, which results from complexities in abstract thinking, memory or language (Coriale et al., 2013). Problems with interpreting cause and effect, understanding and interpreting social cues can result in not being able to process, understand the importance of, or follow rules. Children with FASD may appear to be uncooperative with peers or find it difficult to take turns, may interrupt work and play, or be inappropriately intrusive (Lange et al., 2017). This can result in children finding themselves socially isolated or preferring the company of younger children (Catterick & Curran, 2014). A combination of early childhood trauma, widespread

neural damage, as well as problems with understanding social rules and cause and effect means children with FASD are often labelled as antisocial, callous/ unemotional, aggressive, disobedient or violent (Price et al., 2017). This accounts for the large proportion of children who also meet the clinical threshold for Conduct Disorder, as examined by Popova and colleagues (2016). Many of these behaviours become more apparent when the child starts school and finds social situations and academic instructions difficult. It is unsurprising therefore the high prevalence of Conduct Disorder in this population. Children with FASD can find themselves feeling misunderstood, while navigating seemingly complicated social rituals and distressing home and school environments. A lack of educational guidelines or awareness amongst teaching staff means children with FASD are often labelled as disruptive and removed from their learning environment, while many teachers in the UK currently do not receive training around teaching a child with FASD (Price et al., 2017; Williams et al., 2012).

By adolescence, facial characteristics tend to become less pronounced but short stature and microcephaly remain (Mukherjee, 2019). Adolescents with FASD tend to complete less formal education than their TD peers, but it is unclear whether this trend is attributable to socioeconomic status since this is also the case for children in foster care (Price et al., 2017). Adaptive functioning problems, including rule following and understanding social norms tend to permeate into adolescence (Price et al., 2017). Adolescents with FASD are more likely in later life to engage in antisocial behaviours such as stealing, cheating, acting young, as well as sociopathic behaviours (Greenbaum, Stevens, Nash, Koren, & Rovet, 2009). Studies on FASD in adulthood are scarce but it is estimated that children with FASD are 90% more likely to develop mental health problems, 49% more likely to engage in inappropriate sexual behaviours, 60% more likely to fall in trouble with the law, and 33% more likely to have substance abuse and alcohol related problems later in life (Coriale et al., 2013). It is also estimated that 23% of the prison population in the US reaches the diagnostic threshold for FASD, in comparison to 2.4-4.8% of the general US population (Allely & Gebbia, 2016; Allely & Mukherjee,

2019; May et al., 2009).

1.2.2.1 Towards a neurodevelopmental profile

The pathognomonic features of FASD are yet to be identified. Identifying them remains a challenge given the wide range of characteristics individuals with FASD exhibit, or may not exhibit, as well as the fact that many items overlap with other disorders. Such a test must be conducted in a diverse population and have both sensitivity and specificity. Much of the research on the FASD neurobehavioural profile is dominated by validating the Neurobehavioural Screening Tool (NST) which is currently used to screen general populations of school children in order to identify those with a higher chance of having FASD (See Table 1.3; Lange et al., 2017; Nash et al., 2006; Stevens, Nash, Koren, & Rovet, 2013).

1.2.3 Prevalence

The most widely referred to prevalence statistic is that FASD is present in 2.4-4.8% of school aged children in the USA, Canada and some Western European countries (May et al., 2014, 2018, 2009; Popova, Lange, Probst, Gmel, & Rehm, 2017). The accuracy of this statistic is dependent on the validation of prevalence methodologies. The figure quoted by May, Popova and colleagues (2009; 2014; 2017; 2018) was reached through the analysis of several active case ascertainment studies that measured FASD symptomology (case histories of alcohol use, facial and cranial dysmorphology, a standard neurobehavioural screening test) in children in primary schools, using school based studies, since these are more representative of the wider population. May et al.'s (2009; 2014) Western European estimate is based on the analysis of two in-school studies completed in Lazio, Rome, where the prevalence was estimated at 2-5.5% in 5-7-year-old children.

Table 1.3: Neurobehavioural Screening Tests for FASD and their Classification Indexes

	Description	Analysis	Classification Index (Sensitivity/ Specificity
Child Behaviour Checklist *(CBCL)* (Reported by Lange et al., 2017)	113 Item checklist	Discriminant Function Analysis	86/82%
Behaviour Rating Inventory of Executive Function (BRIEF) (Reported by Lange et al., 2017)	86 Item checklist	Discriminant Function Analysis	Not recorded: Overall accuracy 71%
Mattson et al., 2010	Battery of tests for FAS: *CANTAB* Cambridge Neuropsychological Test Automated Battery, *D-KEFS* Delis-Kaplan Executive Function System, *MVWM* Morris Virtual Water Maze, *NES3*Neurobehavioral Evaluation System 3	Latent Profile Analyses	87.8/95.6%
Enns & Taylor, 2016	Battery of tests: *CMS* Children's Memory Scale, *D-KEFS* Delis-Kaplan Executive Function System, *WISC-IV* Wechsler Intelligence Scale for Children, Fourth Edition, *WMS-IV*Wechsler Memory Scale, Fourth Edition, *WRAT4* Wide Range Achievement Test, Fourth Edition	Logistic regression	Not recorded: Overall accuracy: 75%
Fetal Alcohol Behaviour Scale (A. Streissguth, Bookstein, Barr, Press, & Sampson, 1998)	36 Item scale marked by someone who knows the participant well	Scale Items weighted	Not recorded: Cronbach's Alpha score: 0.89
Neurobehavioural Screening Tool (K. Nash et al., 2006)	10 Item checklist marked by caregiver	Scale Items weighted	62/100%

Whilst it is fair to rebut, as Pichini did in 2017, that this prevalence statistic is not representative of the wider Italian population (and indeed cannot represent Western Europe where drinking, particularly binge drinking, differs from country to country), it has to be noted that the 36 in-school studies that were analysed by May et al. did follow the increase in pregnancy and drinking trends outlined by the World Health Organization (Pichini et al., 2017; World Health Organization, 2014). Additionally, a follow up study conducted by Popova et al. (2017b) estimated the Western European prevalence rate of FASD at 3.74%, based on World Health Organization figures of maternal alcohol consumption. If indeed these are accurate, this makes FASD the most prevalent form of neurodevelopmental disorder known (Popova et al., 2017).

More recently in the UK, McQuire and colleagues (2019) conducted a large epidemiological study screening for possible FASD in a cohort of 13,495 children born between 1991-1992. They reported that 79% of pregnant women admitted to drinking at some point during their pregnancy and calculated that between 6-17% of the cohort would pass a screening test for FASD (McQuire et al., 2019). In comparison, the World Health Organisation reports the UK as having the second highest rate of drinking during pregnancy in Europe, at 29.5% (World Health Organization, 2017). The disparity of clear data in this field means that an accurate prevalence statistic of FASD in the UK is unknown and the most widely used statistic comes from American and Canadian prevalence studies. Barriers to the detection of both the prevalence and incidence of FASD include the lack of reliable and consistent data collection, the difficulty of diagnosing it, and difficulties in gathering information on gestational alcohol consumption (Morleo et al., 2011).

Metabolised FAEE accumulates in meconium, the first stool passed by a new-born. In 2010, Hutson and colleagues tested 900 stratified meconium samples for FAEE, and found that 44% were positive for alcohol exposure above the cut-off of >2nmol/g (Hutson, Magri, Gareri, & Koren, 2010). In a replicated study in Barcelona, 45% exceeded the cut-off (Gareri, Lynn, Handley, Rao, & Koren, 2008). This is five times more than reported in self report questionnaires. Additionally, placental FAEE levels are elevated in pregnancies that result in premature delivery (Gauthier et al., 2015). Such biomarkers would help in identifying FASD in children, and currently meconium – and umbilical cord – testing is conducted only when a primary physician or social worker suspects either inter uterine drug or alcohol exposure (Himes et al., 2015). A large scale stratified meconium testing study, replicating the two studies mentioned above, is currently taking place at Glasgow University (NHS Health Research Authority, 2020).

As a comparison, the prevalence of diagnosed Autism can confidently be placed at 1%, and the estimated prevalence of all diagnosed and undiagnosed Autism at 1.57% (Baron-Cohen et al., 2009). This is known because a number of school based population studies, analyses of the Special

Educational Needs and Disabilities registers, an estimation of known/ unknown cases in the general population, a UK household survey of 7,500 adults, and epidemiological reports from the Department for Education Public Health England have been undertaken in order to measure Autism prevalence (Baron-Cohen et al., 2009). It, however, remains an area of much needed further research in FASD.

1.2.3.1 Environment and other influences

Whilst PAE is its common denominator, the additional consequences incurred by prenatal drug use, pre and postnatal environmental stressors and maternal and fetal epigenetics also contribute to the neuronal development which eventually becomes FASD (Hellemans, Verma, et al., 2010; Lussier, Weinberg, & Kobor, 2017). Ninety percent of prenatal alcohol exposure co-occurs with multiple drug use, environmental or socioeconomic stress, mental health problems, abuse, neglect, experiences with criminal justice, welfare or child protection services (Fast & Conry, 2009; Price et al., 2017; Thanh, Jonsson, Moffatt, & Dennett, 2013). Eighty percent of children with FASD are brought up in foster or adoptive care (Burd, 2001), and the UK care system is estimated to have a prevalence of around 30% of children with FASD (Price et al., 2017). This creates additional early life traumas which, in children, can result in several behavioural, affect-related, or cognitive issues, but in children with FASD interact with damaged neuronal structures. Put together, these early life traumas can create complex and non-syndrome-specific neuropsychological difficulties in children. Studying FASD is therefore complex because not only is there no distinct neurodevelopmental profile, but when taking into consideration behavioural difficulties due to prenatal alcohol consumption, clinicians must also take into consideration each child's individual early life experience. *Any* extrapolations of the direct involvement of alcohol on the neurodevelopment of a child must take these contributory factors into account.

1.2.3.2 Societal Impact and Importance

With an estimated 35% of children in foster care (Gregory, Reddy, & Young, 2015), 23% of the prison

population (Allely & Gebbia, 2016), and 2.4-4.8% of children in schools estimated to have FASD, together with serious secondary sequelae and poor long-term health, labour and socioeconomic outcomes, FASD is a major public health concern. The cost of FASD is currently estimated at £2bn (Mukherjee, 2019), however this estimate is taken from two US studies and the figure used is converted from dollars. It is a widely used statistic since it is the only available cost estimate but is not completely accurate since both the prevalence and the costs of the services involved differ in the UK and the US. In 1991 the annual cost of FASD was estimated to be approximately $75m in the US. In 2002, it was estimated at $3.6 billion in the US (Lupton, Burd, & Harwood, 2004) and C$2.3 billion in Canada (Popova, Lange, Burd, & Rehm, 2016). Costs accrue from: physical and financial stress of the caregiver; family social service support; family key worker support; child's education plan; child mental health treatment; managing the child's secondary physiological conditions; specialist NHS services; and the estimated loss of productivity, which is the highest contributor to the annual cost. A full review of the societal costs and social impact of FASD, similar to ones carried out in the US and Canada, is much needed in the UK.

1.2.4 Sleep and FASD

Sleep problems are commonly documented in this population and are an important facet of FASD study since many of the behavioural, adaptive and cognitive problems arising from FASD could be associated with sleep problems. Whilst other environmental stressors or influences may also form part of this association, many problems generally associated with insufficient sleep also form the core behavioural, cognitive and affect related problems in FASD.

In recent decades, interest in the long-term outcomes for children with FASD has increased. Several studies that set out to assess behavioural, psychopathological, psychosocial, educational, forensic or socioeconomic outcomes identified sleep problems as a common theme. Steinhausen & Spor (1998) for example examined a cohort of children with FASD (*n*=158) at three separate time points:

preschool, middle school and adolescence through psychiatric interviews, behaviour checklists for parents and teachers, and intelligence tests. In this sample, sleep consistently appeared as significantly problematic throughout the three time points. Importantly, sleep problems appeared to worsen over the period of the study (Steinhausen & Spohr, 1998). In a similar cross-sectional study assessing risk factors for adverse life outcomes in adolescents with PAE, Streissguth et al., (2004) found that over 50% of their sample (*n*=472) identified as having sleep problems, among a number of behavioural and social outcomes (Streissguth et al., 2004). A US Chart review (*n*=2231) conducted by Bhatara and colleagues (2006) of young people at high risk of prenatal alcohol exposure found that 52% were identified as having a 'sleep problem', as identified by behavioural and psychometric checklists (Bhatara, Loudenberg, & Ellis, 2006). A 2009 study by Green et al. in Canada found that 62% of children with FASD aged between 8-15 (*n*=89) were identified as having 'sleep problems', compared to 11% of controls, and sleep problems were one of the most prevalent co-occurrences (Green et al., 2009). These studies were not designed to identify sleep problems but did establish they are prevalent amongst this clinical population. None, however, used validated sleep measures to assess sleep problems.

Research focussing specifically on sleep in FASD continues to emerge. Cross sectional findings from Stade and colleagues (2010) found that children with FASD (*n*=100) have significantly shorter sleep duration than typical controls, and 55% have more than two night wakings as measured by the Pediatric Sleep Questionnaire (Stade et al., 2010). Keiver et al., (2013) conducted clinical interviews with caregivers of 43 children with FASD, finding that 67% had significant sleep problems, particularly with sleep onset, sleep maintenance and night waking (Keiver et al., 2013). In an unpublished study by Chen and colleagues, presented as conference proceedings in 2006, 85% of a sample of children with FASD (*n*=36) who had been referred to their paediatric clinic reached the cut off for clinically significant sleep problems, as measured by CSHQ, although there appears to be sampling bias in this study given that the data comes from children who were referred to their clinic for sleep problems

(Chen & Olson, 2006).

To date, two studies using PSG have measured sleep architecture in children with FASD. The first, conducted by Chen et al., in 2012, (*n*=5) showed objective evidence of obstructive apnoeas, fragmented sleep, and mildly elevated CO_2 levels which suggests SDB in this sample. This PSG data was conducted as the result of clinical suspicion, from a sample of children who had been referred to a sleep clinic so inferences from these findings should be interpeted with caution (Chen, Olson, Picciano, Starr, & Owens, 2012). The second is a doctoral study conducted by Shery Goril in 2016 of children and adolescents with FASD (*n*=36) aged between 6-18 years old. This first major study on sleep in FASD found that sleep is fragmented in this population, with high levels of parasomnia (27.9%) and insomnia (16.8%), as well as SDB. Additionally, abnormal melatonin secretion patterns were observed, with 17% presenting with delayed secretion pattern, 8% advanced secretion pattern, 54% with no clearly classifiable secretion pattern and 21% with normal melatonin secretion (Goril, Zalai, Scott, & Shapiro, 2016). There is an obvious paucity of data in this emerging field, and these two PSG studies have notable limitations. Both contain small sample sizes, and the study conducted by Chen and colleagues (2012) contained sample bias. In addition, both used referent control data to yield comparison data.

1.2.4.1 Mechanistic reasons for sleep problems

Circadian rhythms, including sleep and melatonin production are modulated by the suprachiasmatic nuclei of the hypothalamus. These nuclei receive input in the form of dark and light signals, and additionally cognitive environmental information, which in turn influence the timing, duration and quality of sleep (see Section 1.1.3.2). Prenatal alcohol exposure can structurally alter the suprachiasmatic nucleus, which may in turn have an effect on an individual's perceptual/ cognitive functioning and melatonin secretion, resulting in disturbed sleep/wake behaviours (Earnest, Chen, & West, 2001). In the earlier mentioned doctoral study on sleep in children with FASD, dim light melatonin onset (DLMO) testing revealed that 79% of the participants (*n*=24) had either a delayed

secretion pattern, advanced secretion pattern, or no clearly classifiable abnormal melatonin pattern (Goril et al., 2016). Therefore, melatonin therapy at bedtime might correct the circadian rhythm sleep disorders in this clinical population although research on this topic is scarce.

Studies in rodents and zebrafish demonstrate further mechanistic association between prenatal alcohol exposure and sleep. Several theories suggest that prenatal alcohol exposure affects the cerebellar vermis, an area of the cerebellum that receives somatic sensory information via the spinal cord, from proximal body parts. Prenatal exposure to alcohol in mice has resulted in decreased levels of GABA, which is involved in sleep-wake stability. Damage to the circadian system and decreased levels of GABA will usually lead to frequent night arousals since, at a neurological level, sleep-wake states are not recognised. Ethanol exposure in-fetu affects the developing brain's circadian rhythm and regulatory system, and sleep/wake behaviour, particularly during the brain growth spurt of the third trimester (Sakata-Haga et al., 2006). Additionally, these sleep disturbances start early in life and are present throughout the lifespan (Sakata-Haga et. al., 2006). Sleep deficits found in prenatally exposed young adult rats that had concurrent deficits in visual and spatial memory can be treated and stabilised (Stone et al., 1996).

1.2.4.2 Psychosocial risk for sleep problems

Negative extra-utero environments likely increase the risk of sleep disruptions. This stands to reason given the notably high rates of negative or unpredictable caregiving environments in childhood for those with FASD. Children's cultural, racial and psychosocial risk have previously been associated with differences in sleep patterns and parental sleep expectations (Jenni, 2005). Proximal measures of risk, such as chaotic living environments, are associated with sleep problems (Brown & Low, 2008). Socioeconomic status may moderate the impact of sleep disruption on daytime functioning with those experiencing high socioeconomic status somewhat more protected that those with lower (Buckhalt, El-Sheikh, & Keller, 2007).

Deprivation, whether it is social, biological, emotional or perceptual, can lead a child to lose their secure sense of attachment. If an early caregiver is unable to provide a degree of responsiveness, continuous love and support, or the child is removed from the care of their primary caregiver early on in life, their attachment type can be either anxious or avoidant (Marrone, 2014). Children who have experienced trauma early in life can experience reactional distress and can develop defence mechanisms against such distress. With prolonged institutional care, children are likely to develop long term developmental problems, particularly conduct and attentional difficulties (O'Connor & Rutter, 2000). Attachment problems, in TD children, often manifest at night with sleep anxiety – being afraid of the dark for example, not being able to sleep without a parent present, or not being able to get back to sleep after waking in the night. These problems are also present in children with neurodevelopmental conditions, where the underlying cognitive processes compromise the ability to form secure attachments (Davidson et al., 2015; Howe, 2006). Children with FASD often have attachment related issues, which is unsurprising given the high rates of children with FASD in foster care. In turn, these can have an effect on a child's sleeping pattern (Spruyt, Ipsiroglu, Stockler, & Reynolds, 2018).

1.2.4.3 Sleep and daytime function in FASD

The associations between sleep and daytime functioning are now well established (see Section 1.1.4). Whilst a number of studies have documented the type and extent of dysfunction in daytime learning and behaviour among children with FASD, other than the studies contained in this thesis, only one published study has quantitatively measured sleep and daytime behaviour in this clinical population. This is surprising, because sleep fragmentation from various causes has been linked to deficits in attention, response inhibition, memory, maladaptive behaviour, aggression – all of which are areas of importance for caregivers, can become problematic if untreated, and are well documented among children with FASD.

Wengel et al.'s 2011 study in which caregivers of age-matched toddlers (*n*=19) aged 3-6 years completed the CSHQ, The Sensory Profile (Dunn, 1997), a sleep log, and seven nights of actigraphy. T-tests on the questionnaire data between the clinical and control group revealed that sleep problems (composite CSHQ score; *p* = 0.008) and sensory processing deficits (composite sleep profile score; p=<0.001) were significantly greater in the FASD sample. Significant (>0.5) Pearson correlations in the FASD group included bedtime resistance (most related to fine motor perception; Pearson *r* = 0.57, SD=0.15), sleep onset delay (most related to behavioural outcomes of sensory processing; Pearson *r* = 0.62, SD=0.17), sleep duration (most related to: sensory sensitivity; Pearson *r* = 0.64, SD=0.19 and behavioural outcomes of sensory processing; Pearson *r* = 0.74, SD=0.16), night waking (most related to: modulation of visual and emotional input; Pearson *r* = 0.66, SD=0.15) and parasomnias (most related to sensory seeking behaviour; Pearson *r* = 0.61, SD=0.19). Significant (>0.5) Pearson correlations between sensory profile subscales and actigraphy parameters revealed that wake time/ sedentary (Pearson *r* = -.57, SD=0.19), sleep onset/low endurance (Pearson *r* = 0.52, SD=0.21), sleep efficiency/auditory (Pearson *r* = -0.63, SD=0.13) and mean total activity/sedentary (Pearson *r* = -0.66, SD=0.17) were significantly correlated. Regression data were not used and due to the small sample size, children were age matched with no covarying data (such as sex or SES). R^2 values were not reported (Wengel, Hanlon-Dearman, & Fjeldsted, 2011).

One unpublished study conducted by Chen & Olson was taken from a presentation at the Research Society for Alcoholism, Seattle, in 2006. Caregivers of (*n*=34) children aged 6-12 with FASD completed the CSHQ, and the Behavior Rating Inventory of Executive Functioning (BRIEF), in order to assess day to day behaviours reflective of executive functioning domains. Sleep insufficiency was significantly correlated with Inhibition (p=0.013), Working Memory (p=0.014), and Global Executive Composite (p= <0.001) (Chen & Olson, 2015).

Two further studies were conducted by our group (Mughal & Dimitriou, 2017; Mughal, Joyce, Hill, & Dimitriou, 2020). The former is a published conference (poster) proceeding outlining a pilot study

assessing sleep, language acquisition and maladaptive behaviour in a small sample (*n*=16) of toddlers (aged 18-36 months) with FASD and age matched typical controls. Caregivers were given the Brief Infant Sleep Questionnaire (BISQ), the McArthur Communication Development Inventory (MCDI), and the Child Behavior Checklist (CBCL). Regression analysis showed that a proportion of the variance in the score for the number of words produced and understood, as measured by the MCDI, was attributable to night sleep duration as measured by the BISQ (R^2 =0.152, p= 0.05), and that a larger proportion of the variance CBCL score, indicating maladaptive behaviour, was attributable to sleep duration (R^2 =0.302, p= 0.005). The latter is a study which is outlined later in this thesis as part of Chapter 2, assessing anxiety and sleep in school-aged children with FASD (See Section 2).

There remains a paucity of data in the field of sleep and correlates in FASD, yet this is now understood to be an important area of therapeutic concern. When the first longitudinal and large cross-sectional studies assessing FASD and its related psychosocial outcomes emerged 22 years ago, sleep was a common clinical concern. Both clinical and anecdotal evidence points to the need for sleep intervention data in this population, which is especially pertinent given the cognitive, social, emotional and behavioural sequelae of this population, and the relationship between cognitive, social, emotional and behavioural processes and sleep.

1.2.4.4 Sleep interventions

Current sleep promotion techniques for children with FASD are based around sleep hygiene practices, including sleep scheduling, sleep promoting activities and improving the sleep environment. To my knowledge, one peer reviewed article has been written which outlines sleep intervention techniques for children with FASD. In a narrative review on sleep intervention practices, Jan, Asante, Conry, Fast, Bax et al. (2010) outline a qualitative description of the clinical experiences of professionals working with children with FASD and their caregivers, how sleep hygiene is introduced to caregivers, and what sleep hygiene practices are used. The authors note that each intervention must be tailored to children

individually depending on the child's neurocognitive profile (and may not always work) however minimising perceptual 'noise' in the sleep environment, minimising items that increase sensory and tactile sensitivities (such as tags on pyjamas, textures of bedding, certain sounds or smells) and promoting relaxing bedtime routines can sometimes help caregivers of children with FASD (Jan et al., 2010). However, sleep hygiene techniques often fail to correct sleep disturbances in children with FASD due to an impaired understanding of environmental cues, overstimulation or an inability to relax in ways that TD children can (Jan et al., 2010). Caregivers additionally may not recognise the efficacy of sleep interventions. There is currently no documentation or validated research on the promotion of sleep health for children with FASD and it is not fully known to what extent sleep hygiene interventions are effective (Jan et al., 2010). This demonstrates a need for further research in this area.

1.2.5 Summary

FASD is a multifaceted condition that is widely unrecognised in the medical or educational community. It is thought to be highly prevalent, particularly in Western countries with socially relaxed rules around alcohol during pregnancy and presents with a large range of secondary sequelae relating to memory, affect and attention. Sleep and sensory problems are also common in children with FASD, and many of the functions of sleep are also part of the neurocognitive make-up of FASD.

1.3 Autism Spectrum Conditions (ASC)

Autism Spectrum Conditions (ASC, hereby 'Autism') are characterised by a pattern of social, communication and repetitive behaviours apparent in the first three years of life and occur in a developmental fashion as the individual matures. Whilst there have been numerous definitions of Autism in the past century, ranging from the socially withdrawn Schizophrenic described by Bleuler (1912), to *Autistic Psychopathy*, and *Asperger's Syndrome* described by Asperger in 1938, or *Autistic Disturbances of Affective Contact* described by Kanner (1943), the current understanding of the neurobiological, behavioural and cognitive aspects of this condition is outlined below (Fletcher-Watson, & Happé, 2019).

1.3.1 Diagnostic criteria

The diagnosis of Autism requires evidence of atypical social and communication behaviours, restricted and repetitive behaviours and interests (RRBIs) and hypo or hypersensitivity. Previous versions of the DSM and ICD specified sub-classifications of Autism, such as Autistic Disorder, Asperger's Syndrome, Atypical Autism, or Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS) however it is now considered that the same underlying condition is shared amongst individuals with a large variation of behavioural presentations.

In the absence of a definitive set of biological markers that are sufficiently sensitive and specific, Autism is defined using behavioural indicators. However, it is not a single condition, and similarly to FASD and other social-emotional-behavioural conditions is broadly considered to be a multi-factorial interaction between genetic and environmental circumstances that manifests in a uniform pattern of social, repetitive behaviour and sensory issues (Górriz et al., 2019). Additionally, there are several characteristics that are intrinsic to Autism, such as sleep problems and atypical attentional capacity, that are not part of its diagnostic schedule. Diagnosis is usually made when a child is three years or older. Earlier diagnosis can be made but has an increased chance of a false positive result, since some

communication, repetitive and social behaviours (RRBI's) that are unique to Autism can also be common in toddlers (Randall et al., 2018).

Like FASD, the diagnosis of Autism is multifaceted and often requires a multidisciplinary team of clinical and non-clinical professionals. The Autism Diagnostic Observation Scale, second edition (ADOS-2, Lord, Rutter, DiLavore, Risi, Gotham & Bishop, 2012) combined with the Autism Diagnostic Interview- Revised edition (ADI-R, Lord, Rutter, & Le Couteur, 1994) are considered the gold standard of Autism diagnosis. The ADOS is a direct observation schedule consisting of four modules of varying developmental and language levels, where one module is administered depending on the child's ability. It is delivered through structured and semi structured activities assessing social and communication behaviours. The ADI-R is a structured interview conducted with caregivers, and assesses social interaction, communication and repetitive behaviour (Fletcher-Watson, & Happé, 2019).

The current diagnostic criteria according to the DSM-V and ICD 11 require evidence of atypical social communication and restricted and repetitive patterns of behaviour, interests or activities. These symptoms must be present in the early developmental period and cause clinically significant impairment in every day functioning, that cannot be explained by intellectual disability (see Table 1.3). The same diagnostic criteria may occur in different forms in each individual with Autism (Pellicano, 2011). Communication difficulties can include completely nonspeaking, speaking but only echoing, speaking fluently with an atypical approach to conversation rules, or not understanding non literal language (Fletcher-Watson, & Happé, 2019). Socially this could be a child who is oblivious to others, socially inappropriate in their desire to want to make friends, but approach social communication in an inappropriate way. Communication delays could be due to intellectual disability, socially anxious selective mutism, or a compulsion related to speaking (Fletcher-Watson & Happé, 2019). RRBI's are often self soothing behaviours; these can be repetitive motor movements, such as flapping, stimming, rocking or foot tapping, or sameness behaviours, such as lining up toys. It may also include black and

white thinking, or a very detailed and extensive knowledge of a particular subject – for example calendrical calculation (the ability to calculate which day of the week any given date in history fell on) (Hundley, Shui, & Malow, 2016). Some RRBIs can be complex, rewarding, motivating, self-sustaining or promoting a form of self-expression or creativity (Diener, Wright, Smith, & Wright, 2014; Pring, Ryder, Crane, & Hermelin, 2012). They may be a behavioural manifestation of anxiety and a response to difficult to comprehend situations, or they may add an element of control to the world and reduce anxious feelings (Fletcher-Watson, & Happé, 2019).

1.3.2 Neurodevelopmental profile

In an attempt to delineate the parameters of its neurodevelopmental profile, Morton and Frith's Theory of Autism provides a framework by which cognitive, neurobiological and behavioural insights can be organised (Fletcher-Watson & Happé, 2019b; Lombardo, Lai, & Baron-Cohen, 2019). This framework has been applied both to Autism and more recently by Kodituwakku & Kodituwakku (2013) to FASD. A condition may be diagnosed using a biomarker but can manifest in various cognitive or behavioural features, for example Fragile X Syndrome is identified by a mutation on the X chromosome, but results in a variation of behavioural and cognitive features for which there is no uniform profile (Morton & Frith, 1995). Secondly, a condition may have multiple biological causes, no uniform behavioural manifestations, but a specific cognitive outcome: for example dyslexia, where developing neural pathways diverge from typical formation in the visual-auditory-phonological cortical loops, result in no behavioural manifestations, but one single cognitive manifestation of problems with word decoding and reading comprehension. Thirdly, a condition can have any number of neural or cognitive bases, but only one behavioural outcome, for example Conduct Disorder, which has a number of aetiological features but a single behavioural manifestation (Fletcher-Watson, & Happé, 2019). It appears that Autism is the behavioural manifestation of several neural, environmental and cognitive processes without a simple profile, with research continuing to emerge on both its pathognomonic as well as behavioural features (Fletcher-Watson, & Happé, 2019).

Table 1.4: Autism Diagnostic Criteria, DSM-V

A.	***Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history:***	**A.i**	Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
		A.ii	Deficits in nonverbal communicative behaviours used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
		A.iii	Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behaviour to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers. *Specify* current severity: Severity is based on social communication impairments and restricted repetitive patterns of behaviour.
B.	***Restricted, repetitive patterns of behaviour, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text):***	**B.i**	Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
		B.ii	Insistence on sameness, inflexible adherence to routines, or ritualized patterns or verbal nonverbal behaviour (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat food every day).
		B.iii	Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interest).
		B.iv	Hyper- or hyporeactivity to sensory input or unusual interests in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement). *Specify* current severity: Severity is based on social communication impairments and restricted repetitive patterns of behaviour.
C	**Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities or may be masked by learned strategies in later life).**		
D	**Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.**		
E	**These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and Autism spectrum disorder frequently co-occur; to make comorbid diagnoses of Autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.**		

1.3.2.1 Biological explanations of Autism

1.3.2.1.1 Evidence from genetics

There is evidence to suggest that Autism is the result of a combination of hereditary, environmental and epigenetic factors, however at present definitive biomarkers are yet to be discovered (Muhle, Reed, Stratigos, & Veenstra-VanderWeele, 2018). Seminal twin studies show Autism to be present in higher concordance in monozygotic than dizygotic twins (Le Couteur et al., 1995), with a higher heritability likelihood in later parity/gravidity (Tick, Bolton, Happé, Rutter, & Rijsdijk, 2016). There are many candidate genes that are likely to be part of the Autism genetic makeup, but confidently discriminating one or a set of genes responsible for all variants is unlikely given the wide range of aetiological markers. It is likely that Autism is the product of a large number of genetic common variants, each of which have a small effect, or a construction of 'polygenic scores' which identify a combination of familial or 'de novo' genetic variants (Serdarevic et al., 2020).

1.3.2.1.2 Structural neuroanatomy and neural connectivity

Several candidate neuroanatomical locations have been researched in relation to their relevance to the characteristics of Autism. The amygdala and prefrontal areas for example are involved in social and aggressive behaviours, as well as eye gaze and face processing (Park et al., 2016). Lesions to the amygdala in non-Autism populations results in abnormal fear processing, modulations of memory with emotional content, and eye gaze when looking at a human face (Spezio, Adolphs, Hurley, & Piven, 2007). The amygdala receives highly processed somatosensory, visual, auditory and autonomic input and its function is associated with Autism. Lesions in the amygdaloid nucleus result in some compulsivity symptomology that is characteristic of Autism (Park et al., 2016). Temporal lobe tumours involving the amygdala and hippocampus can result in Autism-like traits (Taylor, Neville, & Cross, 1999). The frontal lobe, which is involved in higher order cognitive processing, language, social and emotional function, is also considered to be relevant to the Autism profile. Some of the more

replicated neurobiological findings in Autism look at early brain overgrowth in the first four years of life. Normal cell death, and neuronal competition are disrupted in early childhood and result in an accelerated growth pattern seen in a minority of children (Zwaigenbaum, 2014). This growth mainly relates to frontal cortex volume (Courchesne et al., 2011). Finally, the nucleus accumbens is considered a key structure related to social reward responses in Autism, when working in cortical loops with the ventromedial prefrontal cortex, putamen, amygdala and/ or caudate. Studies using Functional Magnetic Resonance Imaging (fMRI) found that, in neurotypical individuals, Theory of Mind (ToM) tasks activate prefrontal, temporal as well as parietal areas, whilst in individuals with Autism, ToM tasks showed reduced or less coordinated global activity, whilst 'at rest' states showed increased activity (Padmanabhan, Lynch, Schaer, & Menon, 2017).

Studies exploring the structural formation of various neuroanatomical regions in Autism have shown significant differences in the sizes of frontotemporal, frontostriatal (implicated in repetitive and stereotyped behaviour) and amygdal areas of individuals with Autism when compared to neurotypical individuals (Nickl-Jockschat et al., 2012). However, such differences in size cannot be attributed to causation; it is unclear whether an individual with Autism has increased repetitive behaviour because of a larger frontostriatal structure, or whether the repetitive and stereotyped behaviour has strengthened the neural connectivity in the frontostriatal structure, thereby making it larger in size. For example, anxious individuals are more likely to have a structurally different amygdala, whilst London taxi drivers, who have extensive navigation experience, are more likely to have structural differences in the posterior hippocampus, which is involved in the recognition of the spatial environment (Maguire et al., 2000).

Besides neuroanatomical structure size, research has focussed on structural connectivity. It is widely considered that the biological marker for Autism will be defined by synaptic functioning (Ameis & Catani, 2015). Atypical GABA and glutamate signalling are thought to key to the pathological

mechanisms of Autism (Horder et al., 2018), which may in turn impact local and global synaptic connectivity (Ameis & Catani 2015).

1.3.2.2 Cognitive profile of Autism

1.3.2.2.1 Theory of mind

The ability to independently attribute mental states to oneself and others in order to explain behaviour is referred to as Theory of Mind (ToM; Premack & Woodruff, 1978). ToM addresses meta-representational deficits in Autism, between two mental states that are independent of each other, for example an opinion, knowledge, or belief. ToM measurements such as false belief tasks of judgement indicate an inability to judge other mental states and are shown in higher rates in the Autism population and is conceptualised as a deficit in metarepresentation (Baron-Cohen, Leslie, & Frith, 1985).

Variants of ToM include attention and visual tracking, to look at focus and intentions, which in turn can reveal information about dyadic interactions. Dyadic interactions with a third focus or interaction (for example a parent and child [dyad] looking for a butterfly [third focus]) provide the basis for a Shared Attention Mechanism, which is conceptualised as a cognitive basis of ToM (Baron-Cohen & Goodhart, 1994). More recently, eye tracking tasks which measure the point of gaze, eye positions and eye movement, have been used to assess mentalisation in TD children and those with Autism, finding that saccadic movements in TD children were more likely indicate anticipated behaviour on the basis of false belief (Farnsworth, 2018; Senju, Southgate, White, & Frith, 2009).

Research on gestures in early typical and Autism development found that metarepresentational deficits resulted in reduced gestures in toddlers with Autism (Attwood, Frith, & Hermelin, 1988). Attwood et al. (1988) found that the reduced gestures (for example pointing or clapping) revealed an atypical understanding of other mental states, resulting in little or no gestures expressing consolation, embarrassment or goodwill, but an increased amount of gestures around behaviours where

something is needed, such as 'be quiet, come here, go away' or relating to sensory needs rather than social needs (Attwood et al., 1988). Baron-Cohen and Goodhart, (1994) constructed from this the model of pointing in early Autism, finding that children rarely point to share (protodeclarative pointing) and were more likely to point to get a desired object (protoimperative pointing).

However, age, cognitive ability, and the presence of a neurological condition other than Autism can affect the outcome of a false belief task. ToM cannot therefore be used as a predictive measure of Autism since it does not yield a high enough sensitivity or specificity. For example, individuals with a diagnosis of Schizophrenia, ADHD or with right hemispherical damage also tend to fail Happe's Strange Situation task, a false belief task for adults in which individuals are given short descriptions of a scenario resulting in a non-literal untruth (Fletcher-Watson & Happé, 2019b).

1.3.2.2.2 Executive function

Executive functioning is responsible for a large amount of higher order tasks and processes and are mediated by frontal lobe function (See Section 2.1.2.3 for a review). Executive functioning includes planning, impulsivity, initiating activities, inhibition, working memory, shifting from one task to another or organising the surroundings and are linked to prefrontal activity. Autism is widely conceptualised as a deficit in executive function (Hill, 2004). For an individual to perform an executive function task, they firstly need to disengage from the immediate environment and guide actions or instructions that may not be immediately obvious (Fletcher-Watson & Happé, 2019b). Neural damage to the frontal lobes caused by traumatic brain injury can result in atypical executive function, as well as other neurodevelopmental conditions which result in atypical frontal lobe structure, such as ADHD, Obsessive Compulsive Disorder, Tourette's Syndrome, FASD and Schizophrenia (Ozonoff & Jensen, 1999; Sergeant, Geurts, & Oosterlaan, 2002). Behavioural manifestations of executive function difficulty can include rigidity of behaviour, fewer behavioural examples of initiating non routine actions, the tendency to become engrossed in an activity, a liking for repetitiveness, or elaborate

rituals. These may come to dominate the daily life of some individuals and may need prompts to initiate changes in a routine. Children may tend to forget things or find a list of objects or instructions difficult to both remember and attend to. They may appear to be disorganised but attempt to overcome this through lists or adhering to rigidity and structure (Fletcher-Watson & Happé, 2019b).

An executive function model of Autism can explain social difficulties, as well as operationalised false belief. This is because executive function functions across many different domains (Yerys, Hepburn, Pennington, & Rogers, 2007). One task examining this hypothesis is the 'Windows Task' in which a child has to point at one of two boxes, which have small windows, into which only the child is able to look. One box contains a sweet, while the other box is empty. If the child points at the empty box, they will get the sweet. Subsequently a competitor is introduced. When the competitor points to the box that the child points to, the competitor wins whatever is in the box, which results in the child winning sweets deceptively. Children with Autism are more likely to score incorrectly on this task: there may be a difficulty in overcoming the perceptual salience of an object; there may be a difficulty in prioritising a mentalising task over inhibiting actions towards a desired object (Yerys et al., 2007).

Similarly in the Tower of Hanoi task (a mathematical puzzle in which a series of discs must be moved in a certain order, widely used to measure executive function), children with Autism are more likely to detour, act away from the object, or show difficulty in inhibiting a previously rewarded response (Hughes, Russell, & Robbins, 1994).

Executive functioning deficits may additionally contribute to social interaction and communication difficulties, but these are not limited to Autism and similar profiles of social/communication/executive function can be seen in other neurodevelopmental conditions (Happe & Fletcher Watson, 2019). For example, as mentioned in Section 1.2, children with FASD present with processing problems which fall under the umbrella term of executive function. On the other hand, there are a number of individuals with Autism who are able to socially 'camouflage' their Autism traits which requires a sophisticated

understanding of social behaviour and therefore high levels of both executive function and ToM (Happe & Fletcher Watson, 2019). Executive function therefore cannot be used as a stand-alone measurement or indicator of Autism, but can provide some indication that Autistic traits are present.

1.3.2.2.3 Weak central coherence

Central Coherence refers to the tendency to draw many pieces of information together and form a whole; an ability to view and observe situations, objects or concepts as a part of a bigger whole or overall meaning (Pellicano, 2011). Experiments that focus on minute details, such as the Block Design and Integrated Figures tasks demonstrate that individuals with Autism tend to overlook the bigger picture but have a keen eye for detail within the picture. This indicates more focus and attention on local rather than global processing (Shah & Frith, 1993). Such observations on attention to detail were noticed by Kanner in 1943, who noted that children had the inability to process wholes without full attention to the constituent parts, and when one of the parts was taken away, it altered the whole enough to not be considered a whole anymore. This can also be seen in autistic perceptions of meaning. For example, using weak central coherence theory, the sentence “Mary took the dog for a walk, she went to fetch the lead” could be interpreted as Mary fetching the dog’s lead, or Mary fetching lead from a pencil. Central coherence theory is better understood within the framework of the Enhanced Perceptual Functioning Model, described below.

1.3.2.2.4 Enhanced abilities

The Enhanced Perceptual Functioning model looks at the difference between autistic and neurotypical perceptual processing. Individuals with Autism tend to display enhanced local visual and auditory perception, discrimination, and perception of static stimuli. There is an increased use of posterior neural regions in visual tasks, and a decreased perception of complex movement, and higher order processes rely on local information processing. This results in an increase in perceptual expertise,

which could be due to the over functioning of various neural regions (Mottron, Dawson, Soulières, Hubert, & Burack, 2006).

Children that are non-verbal or minimally verbal may be incorrectly assumed to have lower cognitive functioning when tested using language-dependant cognitive assessments. Cognitive assessments designed for TD children may not be valid in a minimally verbal child. Children, for example, who perform poorly on traditional measures of intelligence such as the Weschler Intelligence Scale for Children (WISC-IV) can perform within standard norms when tested with visual search tasks or other visual tests of intelligence such as the Ravens Coloured Progressive Matrices (RCPM). This indicates that cognitive abilities may be underestimated in children with Autism who display less spoken language (Courchesne, Meilleur, Poulin-Lord, Dawson, & Soulières, 2015). Additionally, studies using visual search tasks have revealed that individuals with Autism have an enhanced or superior ability to discriminate, but a diminished ability to generalise. Children with Autism consistently outperform age and IQ matched neurotypical children in certain task searches (O'Riordan, Plaisted, Driver, & Baron-Cohen, 2001), regardless of whether there is perceptual crowding (Shirama, Kato, & Kashino, 2017), but only in the event that they reach other age related expectations (Lindor, Rinehart, & Fielding, 2018). As will be discussed further in Section 3 of this thesis, children with Autism tend to process higher perceptual loads in attentional tasks even when increasing task irrelevant stimuli, which suggests that individuals with Autism have a higher perceptual capacity (Remington, Swettenham, Campbell, & Coleman, 2009).

1.3.2.3 Behavioural profile of Autism

It was previously mentioned that the diagnosis of Autism requires behavioural evidence of a pattern of social and communication, restricted and repetitive and sensory behaviours. These diagnostic behaviours make up the core behavioural profile of Autism, however the same behavioural feature may be present in an individual with different pathological markers. For example, a non-speaking child

may present with significant intellectual disability which has contributed to the significant communication difficulty. Meanwhile, another non-speaking speaking child may present with no intellectual disability, with ability to speak, but a compulsivity around speaking that results in the child being non-speaking (Soulieres & Mottron, 2013). This variability in the underlying cognition behind behavioural manifestations questions the homogeneity of behavioural phenotypes. Additionally, interventions (for example in the classroom) should understand the different underlying pathologies that result in the same pattern of behaviour. Makaton can be used for simple gestures and words for a non-speaking child with an intellectual disability, whilst relaxation techniques can help with compulsivity around speaking (Tager-Flusberg & Kasari, 2013). Furthermore, behavioural presentations of Autism are only as valid as the context in which they are performed. For example, a specialist and all-consuming interest in organic chemistry will not be efficient for most social communication behaviours between peers, but could be useful in an academic context (Fletcher-Watson & Happé, 2019b). The underlying cognitive aspects of Autism are therefore key to both understanding its complex behavioural and biological phenotype, as well as devising interventions that may aid in some of the difficulties presented.

1.3.2.4 Sensory profile

A sensory profile forms part of the core profile of Autism and has recently been added to its diagnostic criteria. Individuals with Autism may experience hyposensitivity, such as the drive for being freezing cold, eating hot chillies or seeking immersive, squeezing sensations; or hypersensitivity, such as extreme aversion to the sound of the vacuum cleaner or the feeling of labels inside clothing scraping against skin. Such hypo or hypersensitivities may not be focussed on physical inputs but may extend to the ability to perceive and interpret visual, auditory and social cues (DeGangi, 2017). It has been proposed that the neural responses to sensory information form the basis of the understanding of Autism (Schauder, Mash, Bryant, & Cascio, 2015). High perceptual capacity might result in irrelevant stimuli being more apparent, and intruding on attention more easily, leading to unwanted distraction

by sensory stimulation (Remington et al., 2009). At the cognitive level this may be understood within an attentional framework, in that there exists a relationship between the focus on details and patterns of sensory sensitivity. For example, there may be a focus on the details of a sensory input: the presence of a specific frequency in a complex audio stimulus -such as the sound of a vacuum cleaner- could make the sound particularly unbearable. Sensorimotor RRBIs appear to be related to sensory symptoms. For example, a child might find the sound of a buzzing lightbulb deafening, but becoming preoccupied with hand flapping might be a way of tuning out the unwanted sound or a way of feeling calm (Fletcher-Watson & Happé, 2019b).

1.3.2.5 Environmental influences

Whilst the genetic influence on Autism is significant, genetically identical twins do not share 100% concordance, suggesting environmental influences may be a factor in its development. Prenatally, there is evidence that viral infections, zinc deficiency, abnormal melatonin synthesis, maternal diabetes, advanced parental age, and pre and postnatal environmental stress increase the likelihood of Autism (Park et al., 2016). Additionally, there is a higher occurrence of Autism in individuals with FASD, which means that PAE may be part of its aetiological load (Mukherjee, 2019; Mukherjee, Layton, Yacoub, & Turk, 2011).

1.3.2.6 Early markers of Autism

Developmental theories suggest that early differences in a child's interaction with their environment support an alternative developmental trajectory, which eventually becomes Autism. It is usually diagnosed in early childhood, with the average diagnosis being made between 34-50 months (Salomone, Charman, Mcconachie, & Warreyn, 2016). Diagnoses are made before the age of three, but these can be highly variable in sensitivity as many of the repetitive behaviours intrinsic to Autism can be viewed as typical toddler behaviour. There is no reliable way of diagnosing one year old with Autism.

There is mounting interest in identifying early signs of Autism within the first year, or prenatally. Early observations may pick up subtleties in an infant's interaction with the social world, motor skill or processing abilities to indicate likelihood of a later Autism diagnosis. Blasi and colleagues (2015) for example tested the cortical sensitivity of a sample of infants aged between 4 and 7 months (*n*=15) who were siblings of children with an Autism diagnosis, with a high likelihood for later emerging Autism. The authors reported that the age matched control group showed early signs of specialisation for human voice processing in the frontal and temporal regions, and stronger sensitivity to sad vocalisations in the fusiform gyrus and hippocampal regions that were not apparent in the high likelihood group (Blasi et al., 2015). Similarly, infants who have a high likelihood of a later Autism diagnosis show atypicality in visual search (Gliga et al., 2015) and motor skills (Leonard, Bedford, Pickles, & Hill, 2015) when compared to age matched TD controls. Retrospective report, parental report and video analysis has additionally gathered some information on early signs of Autism, such as low amounts of smiling and orienting to own name (Palomo, Belinchón, & Ozonoff, 2006). Social Orienting Theory suggests this could result in atypicalities in multiple domains, for example infants less attentive to social stimuli are less likely to attend to social behaviour, facial or voice orientation which can in turn result in missing out on listening to and learning language. This can lead to a lack of comprehension about the social world, that reinforces the alternative attentional trajectory (Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998; DeQuinzio, Poulson, Townsend, & Taylor, 2016).

The Social Motivational hypothesis suggests that social stimuli can be rewarding to infants, and an early sign of Autism may lie in the indifference to seeking social stimuli (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012). Such social behaviour may start off as a preference, but with repetition may entrench into a pattern of behaviour and set of neural pathways. There is evidence to suggest that neural regions that are specifically for the purpose of social interaction are repurposed in Autism (Grelotti et al., 2005).

Attention switching tasks measure the ability of the infant to switch attention from a central target that has disappeared, to a peripheral target that has appeared. They may also measure the switching of attention from the central target to the peripheral target whilst the central target is still in view (gap-overlap score). Higher gap-overlap scores in infants are associated with later Autism diagnosis (Jones, Gliga, Bedford, Charman, & Johnson, 2014). Additionally, eye movements in infancy including shorter attentional fixation lengths (Wass et al., 2015), micromovements of the head (Torres & Denisova, 2016) and distinctive motor movements detected in gameplay (Anzulewicz, Sobota, & Delafield-Butt, 2016) are associated with later diagnosis. Motor development may also be an early sign of Autism with several fine and gross motor movements observed in infants with Autism, that can stem from RRBI and/or sensory behaviour. These include walking on tip toes, a bouncy gait, dyspraxia, repetitive motor and stimming behaviours such as hand flapping, body rocking or finger twiddling (Happe & Fletcher Watson, 2019).

1.3.3 Prevalence

Current prevalence estimates consider Autism to be present in 0.62% of the global population, however there is variability in diagnostic practices and epidemiological research conducted globally, particularly in low-middle income countries (Elsabbagh et al., 2012). The prevalence rate of Autism in the UK population is around 1.1% (NHS England, 2012), and the estimated prevalence of all diagnosed and undiagnosed Autism in the UK is 1.57% (Allison, Auyeung, & Baron-Cohen, 2012). Fifteen percent of UK school children have a special educational need, which includes language difficulty (including English as a foreign language), mental health needs, and language and communication difficulties. Four percent of UK school children have an Educational Health Care Plan (EHCP), and 43% of applications for EHCPs are for Autism (UK Department for Education, 2019).

The prevalence of Autism has increased substantially in the past thirty years due to changes in diagnostic practice and possibly changes in likelihood-increasing environmental conditions (Rutter, 2005). The rise in the diagnosis of Autism is also accompanied by a fall in the prevalence of other neurodevelopmental conditions, such as global developmental delay or intellectual impairment, which suggests that diagnostic substitution (or perhaps greater accuracy of diagnoses) may have contributed to the increase (Shattuck, 2006). Additionally, diagnostic services have reported an increasing number of parents, grandparents and biological relatives seeking diagnosis for themselves following the diagnosis of the child (Happe & Fletcher Watson, 2019).

A significantly higher number of boys than girls are diagnosed with Autism. The current male to female ratio is 4.3:1, however diagnostic practices aimed at identifying Autism in girls is improving (Hull, Petrides, & Mandy, 2020). Historically, a male to female ratio of 10:1 was reported, which decreased to around 2:1 amongst those with intellectual disability (Lord & Schopler, 1987). This was thought to be attributable to various reasons, including the Y chromosome inhibiting gene expression, and females requiring a higher aetiological load to manifest Autism. The definition of female-Autism has changed in recent years and it is now considered that the various social manifestations of Autism look different in boys than girls (Happe & Fletcher Watson, 2019). Fewer diagnosed cases may partly be due to girls being more able to socially 'mask' or camouflage autistic characteristics and therefore evade diagnosis or not raise cause for concern amongst caregivers. This in turn suppresses autistic behaviour such as stimming, RRBs or sensory sensitivity and can explain the increased psychopathology in girls with Autism, which can come about as a result of mental exhaustion (Charman et al., 2011). This is supported by data on the high rates of undiagnosed Autism in eating disorder clinics (Mandy & Tchanturia, 2015) and referrals to mental health services (Duvekot et al., 2017).

1.3.3.1 Co-occurrences

Around 75% of individuals with Autism experience an additional condition, with epilepsy and mental ill health (in particular anxiety, disinhibited and depressive disorders) being the most common co-occurrences, both contributing to early mortality rates (Hirvikoski et al., 2016). Autism also co-occurs with other neurodevelopmental conditions, such as ADHD, sensory processing disorders, FASD, Tourette's Syndrome, and Developmental Coordination Disorder (Abdallah et al., 2011; Kambeitz, Klug, Greenmyer, Popova, & Burd, 2019). Further work is needed to assess the applicability of psychiatric interventions to Autism, since a number of studies suggest that the high rates of psychiatric co-occurrences are due to unrealistic societal pressures (Chevallier et al., 2012; Yafai, Verrier, & Reidy, 2014). Others, such as Wheelwright and Baron Cohen suggest that Autism is part of a 'Broader Phenotype' and exists across a continuum throughout society (Wheelwright, Auyeung, Allison, & Baron-Cohen, 2010).

1.3.4 Sleep in Autism

Sleep problems are as common and as impairing in Autism as sensory issues, and although they are not part of its diagnostic criteria are increasingly recognised by clinicians to be an integral part of the Autism phenotype (Elrod & Hood, 2015; Fadini et al., 2015; Hodge, Carollo, Lewin, Hoffman, & Sweeney, 2014). Sleep problems are often a cause for concern for caregivers and are associated with higher levels of stress and caregiver burden (Levin & Scher, 2016). Whilst there is a lack of comprehensive research in this area, sleep in Autism is a growing field.

Sleep problems in Autism are likely to be influenced by many factors including co-occurring psychiatric conditions such as anxiety or attachment issues which can add to worry around night time or bedtime routines. One contributing factor to sleep problems can be with problems in understanding the social concept of night time, and even in children who display circadian preference for evening time may not fully comprehend or buy into the idea of sleeping at night time. An increasing body of evidence

suggests that endocrine irregularities and gene translation/transcription mechanisms related to sleep may be impaired in individuals with Autism which leads to atypical circadian functioning and dysregulation of day and night functioning (Mazzone, Postorino, Siracusano, Riccioni, & Curatolo, 2018). The process of the transcription of 'Process C' regulating genes (as mentioned in Section 1.1.3.2) BMAL and CLOCK is known to be irregular in children with Autism (Pagan et al., 2017). This, as well as environmental input, may affect the ability of a child with Autism to anticipate circadian changes or adapt behaviour in order to account for changes in the day and night. Adolescents with Autism show irregular melatonin secretion curves which are likely due to genetic or epigenetic factors affecting enzyme regulation of melatonin (Tordjman, Anderson, Pichard, Charbuy, & Touitou, 2005). As well as this, a significant number of individuals with Autism – children and adults – also experience social anxiety, generalised anxiety and internalising behaviour at clinical levels, and so when faced with the prospect of sleeping alone in a darkened room may be inclined to fall into anxious ruminations that can hinder sleep onset. One longitudinal study assessing sleep duration and correlates in a cohort of children with diagnoses of Autism reported that, according to parental report taken from 8 time points between the ages of 8 months and 11 years, children with Autism slept on average 17-40 minutes less than their TD peers, regardless of sex, ethnicity, high parity or epilepsy (Humphreys et al., 2014).

A meta-analysis by Diaz-Roman and colleagues assessed sleep profiles of children with Autism and adolescents taken from objective and subjective studies (Díaz-Román, Zhang, Delorme, Beggiato, & Cortese, 2018). They found that, of the thirty-seven subjective sleep studies that have been conducted in children and adolescents with Autism, bedtime resistance, sleep anxiety, sleep onset delay, night wakings, parasomnias, SDB, daytime sleepiness, restorative value of sleep and general sleep problems were significantly and consistently higher than TD controls. Additionally, children with Autism showed significantly and consistently lower sleep duration. However, and perhaps due to parental bias, there

were no differences in parentally reported problems with sleep efficiency or sleep latency (Díaz-Román et al., 2018).

Of eight studies using PSG measuring a total of 247 participants (*n*=142 Autism, *n* = 105 TD), children with Autism consistently showed lower total sleep time, with an average of 37.5 fewer minutes of sleep per night than TD children and a Standard Mean Difference (SMD) of -0.90 (*p*=0.003); longer sleep onset latency (SMD=0.53; *p*= 0.001); higher amount of time spent in stage 1 sleep (SMD=0.48; *p*= 0.02); a lower amount of time spent in REM sleep (SMD=-0.88; *p*=0.01); lower sleep efficiency (SMD=-1.20; *p*=0.003); and a higher amount of time awake (SMD=0.49; *p*=0.01). There were no significant differences found in the composite scores of stage 2 sleep, SWS, or REM latency.

Of six studies using actigraphy to measure sleep in a total of 276 participants (*n*=143 Autism, *n*=133 TD) the only significant difference that was found in composite scores was in sleep onset latency (SMD=0.80; *p*=<0.001). There were no significant differences in actual sleep, assumed sleep, wake time, or sleep efficiency (Díaz-Román et al., 2018). However, these meta-analytic findings of actigraphy studies are not consistent with the original studies contained within the meta-analysis, or consistent with theoretical models of sleep impairment in neurodevelopmental conditions. Perhaps this is because aggregating scores from various PSG and actigraphy studies that do not use standardised equipment may yield different results, or as the authors suggest, perhaps the results contained here are limited by the co-occurring psychiatric conditions and melatonin or other medication use.

Nonetheless, a relatively sizeable body of literature now exists examining sleep in Autism populations, and sleep and its correlates in Autism populations.

1.3.4.1 Sleep and daytime functioning in Autism

Children with Autism have a high rate of psychiatric comorbidity that can interfere with the regulation of sleep. Clinical levels of anxiety, mood and attentional problems frequently occur in children with Autism which can result in sleep disturbances (Giannotti, Cortesi, Cerquiglini, Vagnoni, & Valente, 2011). This is an important area of concern, given that behavioural interventions can ameliorate the behavioural problems that can be associated with sleep problems. One intervention by Weiksop, Richdale and Matthews (2005) demonstrated the impact of parent training programmes that used behavioural principles to reduce sleep problems in children with Autism, finding that settling problems, night waking and co-sleeping could be reduced through limit setting and reward systems (Weiskop, Richdale, & Matthews, 2005). Another study by Wiggs and France (2000) found that by limit setting and setting rewards during bedtimes, sleep problems such as bedtime resistance, negative sleep onset associations could be reduced (Wiggs & France, 2000). Away from the area of applied behavioural analysis, another therapy that has been successful in treating sleep in Autism (and also addressing underlying principles as well as behaviour) is social story telling. In one single study case analysis by Moore (2004), a sleep intervention was described where a child's own familiar words at bedtime, with attractive pictures, showed the story of relaxing, sleeping and the concept of bedtime. This was successful in creating a new bedtime routine and reinforcing the positive message about sleep behaviour (Gagnier, Moore, & Green, 2011). Another social story intervention demonstrated the reduction in the frequency of disruptive bedtime behaviours in children (*n*=6) with Autism by creating and reinforcing personalised stories about how to manage bedtime problems (Kitchin, 2009). Improving sleep disruption can also improve daytime behaviours, as was demonstrated in one single study case analysis of a girl whose social interaction, auditory sensitivity, focus and repetitive behaviour improved after an adenotonsillectomy (Malow et al., 2006; Malow et al., 2012).

In a minority of children with Autism, sleep problems are associated with early signs of regression. This is when a child appears to develop typically but at a certain point starts to lose speech and social

learning. Between 15-40% of children with Autism 'regress' between the ages of 1 and 3, with a peak at around 24 months, which is when parents tend to first notice the atypical development of their child (Happe & Fletcher Watson, 2019). It is thought that regression occurs during a period of synaptic growth and pruning and is due to a number of genetic influences (Davidovitch, Glick, Holtzman, Tirosh, & Safir, 2000). Over 50% of children with Autism present with at least one sleep problem at the age which coincides with the point of regression (Giannotti et al., 2011). This phenomenon may, as Cortesi and colleagues (2010) suggest, be coincidental, however in one PSG study assessing co-occurring epilepsy in children with Autism, it was found that regression at infancy increased the likelihood of circadian rhythm disorders and epilepsy (Giannotti et al., 2011). This suggests that one of the aetiological factors for sleep problems in Autism is disrupted neural circuitry.

An important reason for intervening in sleep behaviour is to improve daytime functioning. Caregiver reports consistently detail negative behavioural, emotional and cognitive outcomes for sleep deprived children with Autism. Several studies have assessed the association between sleep and daytime functioning in Autism. These have established significant relationships between sleep and challenging behaviour. Fadini and colleagues (2015) found that disorders of arousal, prevalent in 59% of their sample (*n*=45), was significantly associated with social, thought, attentional, aggression, externalising and behavioural problems. Additionally, they found that 59% of their sample met the clinical criteria for sleep disorders (Fadini et al., 2015). Another cross-sectional analysis, of Japanese pre-schoolers (*n*= 965) found that those with a diagnosis of Autism were more likely to have SDB and parasomnias. Sleep problems, particularly short sleep duration, were associated with both internalising and externalising behavioural problems (Hirata et al., 2016).

Various parental questionnaire (CSHQ/Sleep Diary and CBCL) studies have established that poor sleep correlates with behavioural problems in children with Autism. Rzepecka et al. (2011) found that poor sleep accounts for 42% of the variance in challenging behaviour in their group (*n*= 187) of 5-18 year olds with an Autism diagnosis (Rzepecka, Mckenzie, McClure, & Murphy, 2011), while Patzold (1998)

found that difficult daytime behaviour correlates with co-sleeping with a parent (r=0.40; p=<0.01) night waking (r=0.49; p=<0.01) and total behavioural scores (r=0.37; p=<0.01), and Malow (2006) found that affect (r=0.63) and aggression (r=0.47) correlated with poor sleep. Schreck and colleagues (2004) found in their sample (n=55) of 5-12 year olds that sleep duration was negatively associated with overall Autism scores, stereotyped behaviour and atypical social skills functioning (Malow et al., 2006; Patzold, Richdale, & Tonge, 1998; Schreck, Mulick, & Smith, 2004). These authors all found that sleep disturbances are likely to correlate with internalising as well as externalising behaviours as measured on the CBCL.

Additionally, sleep problems in Autism are significantly correlated to hyperactivity, and aggression (Mayes & Calhoun, 2009), affect (Malow et al., 2006), behavioural and social adaptive difficulties (Sikora, Johnson, Clemons, & Katz, 2012), cognition (Gabriels, Cuccaro, Hill, Ivers, & Goldson, 2005), communication difficulties (Schreck et al., 2004) and academic performance (Limoges, Bolduc, Berthiaume, Mottron, & Godbout, 2013). This is true of toddlers and pre-schoolers as well as adolescents and adults (Mazzone et al., 2018).

1.4 Autism and FASD.

Both Autism and FASD (in particular ARND) are neurodevelopmental conditions which are diagnosed only when certain CNS anomalies are noted, usually by caregivers or educational professionals (Enns & Taylor, 2018). Similarly, within both Autism and FASD, atypical behaviours persist in a developmental fashion and can include neuropsychiatric problems as well as impaired learning, language, memory, social and non-verbal communication. FASD is the result of prenatal environments, compounded by adverse events during infancy and childhood, with a variable impact depending on the timing and severity of PAE, as well as genetic and epigenetic susceptibility. Meanwhile Autism is the atypical manifestation of a pattern of social, communication and sensory behaviours, with possibly a series of aetiological factors. Whilst the two neurobehavioural profiles do not overlap greatly, both contain several complementary characteristics around executive functioning, sensory and affect-related pathologies.

Autism and FASD are among the most common neurodevelopmental conditions. As outlined in Section 1.2.3, the conservative estimate of FASD in the West is set at 2.4%, however a lack of prevalence data in this field means that this is not a confirmed statistic. Section 1.3.3 outlines Autism prevalence at 1.1% in the UK and 0.62% globally (given variability in diagnostic procedures and epidemiological study; Lai, Lombardo, & Baron-Cohen, 2014; May et al., 2009; NHS England, 2012).

There is reason to suggest that PAE is an aetiological agent with the ability to produce, amongst other consequences, a clinical presentation that is consistent with Autism (Mukherjee 2011). A meta-analysis conducted by Lange, Rehm, Anagnostou and Popova (2017) estimated the prevalence of Autism in FASD. Disorder specific random-effects meta-analyses were performed on six studies (total clinical *n*=1029), finding that Autistic behavioural characteristics reaching clinical thresholds were

present in 2.6% of the FASD population (pooled prevalence estimate; Lange, Rehm, Anagnostou, & Popova, 2018).

In a longitudinal study assessing a cohort of children with FASD (*n*=21), Mukherjee, Layton, Yacoub & Turk (2011) found a number of Autistic characteristics within their sample. These were: fetching a simple message by the age of three; delayed echolalia; joint referencing problems; atypical one-sided approach to others; lack of awareness of other's feelings; delays in watching and engaging with peers; delays in developing co-operative and parallel play; lack of curiosity (Mukherjee et al., 2011). This study however was conducted amongst a sample of children referred to a FASD clinic and was therefore not generalisable to the wider population, nor was it included in the previously mentioned meta-analysis conducted by Lange et al. (2017).

A cross syndrome comparison conducted by Bishop (2007) found 34% of children in their sample (n=29) with PAE (not diagnosed FASD) showed autistic characteristics such as social withdrawal and repetitive behaviours, however differed in areas of non-verbal communication, internalising behaviours and peer interaction (Bishop, Gahagan, & Lord, 2007; Morleo et al., 2011). Meanwhile whilst Bishop reports that children with FASD appear to be socially withdrawn, others such as Catterick (2016) and Brown (2018) report high levels of prosocial behaviour that is related to attachment issues arising from frequent changes in caregiver (Brown, 2015; Catterick & Curran, 2014)

The fundamental difference between Autism and FASD neurology is thought to be between structural, functional and connectivity differences. There also appear to be some similarities. Miles and colleagues (2003) for example reported that children with FASD from high alcoholism families were more likely to present with an Autism-like regression period in early childhood, which suggests similar neurological components associated with the period of synaptic growth and pruning that are thought to be the underlying cause for regression (Miles, Takahashi, Haber, & Hadden, 2003). However,

children with FASD present with global structural and functional impairment since PAE can result in widespread CNS damage to the development of the embryo and fetus (Miles et al., 2003). It is this structural loss which appears to underline the behavioural output of FASD, however the variability of the consequences of PAE can result in a FASD profile with several overlapping behavioural features, including (but not limited to) ADHD, conduct disorder, oppositional defiance disorder, reactive attachment, other externalising presentations, as well as (as previously mentioned) some features of Autism (Popova, Lange, Shield, et al., 2016). Meanwhile, Autism appears to be the result of overconnected, high density, short range synaptic communication without structural loss (Happe & Fletcher Watson, 2019). As Remington & Fairnie (2019) suggest, this overconnectivity is the underlying reason for the perceptual overload which eventually presents as Autism.

In summary, whilst there are some similarly occurring behavioural features, this thesis does not maintain the line that Autism and FASD are interlinked or mistaken for each other; they appear to be two separate neurodevelopmental conditions affecting a plethora of psychopathologies, with some overlapping aetiological factors and behavioural presentations.

1.4.1 Thesis Rationale.

Childhood is a period of vast neural growth and repair in which the young brain is subject to continuous modifications in response to the environmental stimuli it is presented with. Children with FASD present with global structural and functional damage caused, at least in part, by ethanol interfering with fetal development (Kodituwakku, 2009). PAE results in not only a vast array of physiological defects including (but not limited to) renal, cardiac, pulmonary and visual problems, but also cortical connectivity issues as well as structural damage to subcortical areas. This results in a vast number of behavioural traits including (but not limited to) those that transect Autism (Popova, Lange, Shield, et al., 2016). This is not to say that the profiles of Autism and FASD overlap or are mistaken for each other, but that the phenotypic behavioural characteristics that make up the Autism profile are also picked up, in a small way, by the developing PAE compromised brain (Mukherjee et al., 2011). An understanding of this entire process is crucial to the exploration of the atypical development that is eventually recognised as Autism or FASD; studying the two side by side can offer theoretical explanations of aetiology and developmental profile. Section 1 of this thesis outlines the 'information consolidation' function of sleep. Section 2.1 outlines the relationship between sleep, executive functioning, behaviour and anxiety, whilst Section 3.1 outlines the relationship between sleep, attention, working memory, receptive vocabulary and fluid intelligence. This thesis aims to make the argument that sleep is crucial to the neurodevelopmental process, and is used as a variable here in order to assess the extent to which it plays a part in some of the core pathological aspects of Autism and FASD.

One reason for this particular combination of conditions is because it is important to ask the question, as Mukherjee and Colleagues (2011) do, of whether there is a relationship between prenatal environments and the neurodevelopmental pathways that later manifest as Autism. This can inform

theories of Autism aetiology, at least in part, of the role of prenatal environments and stresses may have (Mukherjee et al., 2011).

Secondly, as mentioned previously, there are behavioural similarities between Autism and FASD. This is because FASD encompasses an array of behavioural presentations, most notably attention and memory issues as a result of PAE induced cortical thinning (Brown et al., 2018). As a result, FASD has several behavioural and cognitive features that are often mistaken for ADHD, oppositional defiance disorder and conduct disorder (Popova, Lange, Shield, et al., 2016). These are externalising conditions which often present as comorbidities to more global and pervasive conditions. Whilst future studies would benefit from assessing ADHD alongside Autism and FASD, the rationale for the present cross syndrome comparison was to compare two pervasive spectrums which present with pathologies spread across several domains.

Thirdly, in finding differences between the two profiles, the work conducted within this thesis can contribute to the growing body of literature examining syndrome specificity in Autism and FASD. There is therefore an emphasis in this thesis on what is conceptualised as 'syndrome specificity', which is only used to describe statistically significant differences (between the two clinical groups and between the clinical groups and the TD group) in the samples used within the current dataset. Generalisations to the wider population are made tentatively and with the support of meta-analytical data.

Fourth, there is a vast amount of literature examining Autism, which is more of a developed field of study than FASD (Lange et al., 2018). Studying Autism alongside FASD makes it possible to identify gaps in FASD literature and make the argument for the allocation of funding to this field. Additionally, it can raise the profile of FASD by setting it alongside a more well-known and well-established field,

whilst also utilising/ adjusting literature and resources available for Autism for a more FASD-friendly audience.

1.5 Chapter Summary

This chapter has provided a broad summary of sleep, FASD and Autism. It is apparent that sleep is somehow intrinsic to development and healthy physiology and neuropsychology in children. Sleep is associated with various daytime functions in children with FASD and Autism alike. These associations are broad and cover many daytime functions. Additionally, there appear to be several similarities between FASD and Autism, perhaps since both conditions are cognitive, social, behavioural and emotional in their manifestations.

In the following two chapters, two experimental and psychometric studies are reported which assess the relationship between sleep and various cognitive and affective domains in children with diagnoses of FASD or Autism, as well as TD children. Each chapter begins with a short literature review on the specific neuropsychological domains relevant to the study, the theoretical motivations for the parameters used, and an overview of missing literature or areas of further enquiry. This is followed by methodology, results and discussion chapters.

Chapter 2

Study 1: Sleep, anxiety, behaviour and executive functioning in children on the Autism and fetal alcohol spectrums.

The first study of this thesis is based around two theoretical propositions: that behaviour is the manifestation of a neural system that is underpinned by emotion and executive control (Bowman, 2016; Khonsary, 2017) and that sleep is important for the healthy function of behaviour, emotion and executive control (e.g. Hoedlmoser et al., 2014; Reynaud, Vecchierini, Heude, Charles, & Plancoulaine, 2018).

In recent years, there has been a development in the understanding of executive functioning as a psychopathological construct, with several models proposing that self-regulatory behaviour and cognitive control ('hot' and 'cold', or behavioural and emotional aspects) make up its core aspects. One theory put forward by Kluwe-Schiavon and colleagues (2017) proposes that executive functioning regulates controlled behaviours and the emotional- salience state through a fluid and continuous process, 'troubleshooting' complex cognitive problems, using emotional salience as a mediator and behaviour as an output (Kluwe-Schiavon et al., 2017). Meanwhile a number of correlative studies show that the processes of executive functioning, behaviour and emotion are integral to neurodevelopment, form core neurodevelopmental profiles of FASD and Autism, and are mediated by sleep processes (See Section 2). This study investigates the relationship between sleep, executive functioning, behaviour and anxiety in children with a diagnosis of Autism or FASD, and TD children. Two hundred and seventy-seven caregivers of children aged between 6 and 16 years with diagnoses of FASD (*n*=104), Autism (*n*=68), or TD children (*n*=102) completed the Children's Sleep Habits Questionnaire (CSHQ), the Behavior Rating Inventory of Executive Functioning (BRIEF), the Spence Children's Anxiety Scale (SCAS) and the Child Behavior Checklist (CBCL). To test for covariance and diagnostic validity, the Childhood Autism Rating Scale – Parents Version (CARS), the Neurobehavioural Screening Test for FASD (NST), and a socioeconomic (SES) questionnaire (detailing level of education, ethnicity, geographical area and income) were also administered. This chapter is comprised of a

rationale for this study, its procedures and results, and is followed by a discussion and interpretation of the statistical relationships that were found.

2.1 Introduction

2.1.1 Anxiety

Childhood anxiety is conceptualised as a persistent and chronic mental state in which unpleasant rumination, fear or worry is developmentally inappropriate and causes significant, life altering distress (American Psychiatric Association, 2013). A child with an anxiety disorder typically presents with nervous behaviour such as pacing, rocking, stimming, somatic complaints or obsessions. These are usually accompanied by internalised symptoms, such as withdrawal with the intention of avoiding triggering stimuli, and/or externalised symptoms, such as aggression towards triggering stimuli. Such nervous, internal and external symptoms are coping mechanisms that can help the child feel safe (Farrell, Ollendick, & Muris, 2019; Seligman, Swedish, & Flannery-Schroeder, 2014). Anxiety disorders are classified by the DSM-V into several categories, characterised by the similar but distinct states of *fear* (the mechanistic response to what is perceived to be an immediate danger) and *worry* (a longer term, constant fear of a lurking danger). Separation anxiety, selective mutism, specific phobia, social anxiety, panic disorder, agoraphobia, generalised anxiety, and substance induced anxiety are the disorders currently classified under the category of anxiety disorders in section II of the DSM-V. Previous versions of the DSM included the subsets of Obsessive-Compulsive Disorder, however these are now categorised in the separate DSM-V sections of Obsessive-Compulsive Disorders and Trauma and Stressor Related Disorders. Those pertinent to this study are outlined below.

Separation Anxiety disorder is characterised by fear and anxiety around the separation from attachment figures, to an extent that is atypical in comparison to typically developing children of a similar age. In addition, there may be persistent fear or anxiety around the safety and wellbeing of the attachment figure or fears around events and situations which may cause the separation or loss of the

caregiver. Prevalence is between 0.5-4.1% in the general population (Farrell et al., 2019) and is more common in girls than boys (Christiansen, 2015).

Specific phobias are characterised by irrational and intense fears of certain objects or situations. Whilst things like spiders, the dark, strangers, monsters, etc. are the source of common childhood fears, specific phobias in childhood are diagnosed when a child is unusually distressed by certain stimuli, is unable to calm down despite adequate reassurance, experiences intense, persistent fears and accompanying physiological symptoms, for more than six months. Unlike common childhood fears, the intensity of specific phobias tends to increase with maturity. Specific phobias are more common in girls than boys, have a median onset of middle childhood and have a prevalence of between 0.6-1.9% in the general population (Farrell et al., 2019).

Social anxiety disorder is characterised by an excessive fear of situations in which there is a possibility that others may impose negative evaluations. This often occurs in social activities, when a child may be performing or speaking in front of people, answering questions in class, or being the centre of attention. Children with social anxiety may have problems making friends and in the upkeep of ongoing friendships. Social anxiety disorder is more common in girls than boys, has a median onset of mid-late adolescence and a prevalence of 0.3-1.5% in the general population (Farrell et al., 2019; Rapee, Schniering, & Hudson, 2009).

Panic disorder is characterised by sudden, unexpected panic attacks, followed by a month or more of worrying about further attacks. Panic attacks are episodes of intense fear, accompanied by somatic symptomology such as palpitations, shortness of breath, numbness or feelings of imminent danger. Panic attacks can occur in conjunction with other anxiety disorders, for example accompanied by fear of separation from the primary caregiver. Maladaptive behaviours may be used to avoid panic attacks, for example the avoidance of not only stimuli that cause panic attacks, but also the avoidance of similar or tangential stimuli (Farrell et al., 2019). Panic Disorder is more common in girls than boys,

has a median onset of mid to late adolescence and a prevalence of 2.1-4.7% in the general population (Kim, 2019).

Generalised anxiety disorder is characterised by persistent and excessive worry that covers several domains, for example separation, social worries, and a specific phobia. Its prevalence is between 0.2 – 3.9% in the general population (Farrell et al., 2019).

2.1.1.1 Anxiety and FASD

PAE alters the neural process of fear conditioning in response to stress (Hellemans, Sliwowska, Verma, & Weinberg, 2010). Even situations of mild stress can contribute to the altered neural pathway that results in clinical anxiety in individuals with FASD (Hellemans, Verma, et al., 2010). In rodent and zebrafish models, social avoidance and stress related behaviours are mediated by PAE and genotype (Baggio, Mussulini, de Oliveira, Gerlai, & Rico, 2018) whilst PAE in the first and second trimester are associated with lower rates of anxiety behaviour than the third trimester (Baculis, Diaz, & Fernando Valenzuela, 2015). In individuals with diagnoses of FASD, this is evidenced in several large-scale studies. In a study of 473 adults with a diagnosis of FASD, 90% of respondents experienced mental health problems, of which depression and anxiety behaviours were major contributors (Streissguth, , Barr, Julia Kogan, Bookstein, 1996). Children with FASD are not likely to remain with their biological parents and often experience maternal separation as well as multiple foster placements, resulting in increased prevalence of separation anxiety disorder (Alberry, Castellani, & Singh, 2019; Alberry & Singh, 2016; Svetlana Popova, Lange, Burd, et al., 2016). Generalised anxiety disorders, as well as symptoms of panic and phobia are positively correlated with PAE and mediated by early life trauma (Price et al., 2017). Clinical anxiety occurs in around 60-80% of children with FASD, and in adulthood, anxiety is a contributor to the major depressive and suicidal behaviours which are the most common causes for admission into inpatient care (Mukherjee, 2019).

2.1.1.2 Autism and anxiety

It is widely accepted that anxiety is an intrinsic feature of Autism, however whether it is a comorbidity or part of a set of pathognomonic features is disputed (Zainal & Magiati, 2019). In both seminal articles that first described Autism, written by Kanner (1943) and Asperger (1944), anxiety is mentioned as a common occurrence. Social fear, worry, obsessive thoughts and behaviours, the compulsive need for sameness and phobias were all described as auxiliary and intrinsic features (Asperger, 1944; Kanner, 1943). However, the exact prevalence of anxiety in Autism is disputed because of diagnostic complexities. In order to correctly diagnose anxiety, symptoms must significantly alter everyday functioning, but on the other hand everyday functioning is already altered due to the presence of Autism (Magiati et al., 2016). For example, social anxiety, avoidance or ritualistic behaviours that help to placate feelings of anxiety overlap both the diagnostic features of anxiety and Autism. Similarly, school refusal in the general population is an indication of separation anxiety, but in a child with Autism can be due to sensory overload, change in routine, social anxiety or a number of reasons that would not be applicable to school refusal in the TD population (Davis, White, & Ollendick, 2014). When measured in the typical sense (without scrutinising the related Autism traits), anxiety disorders are thought to be prevalent in between 50-79% of individuals with Autism (Kerns & Kendall, 2012). Although there is variability depending on the severity of the Autism diagnosis, up to 37% of children and adolescents with Autism meet the diagnostic criteria for OCD, 29.2% for social anxiety, 15.5-20% specific phobia, 19% separation anxiety and up to 70% generalised anxiety which overlaps various specific anxiety disorders (Davis et al., 2014). As with the general population, anxiety is reported to be more common in girls than boys, and has a significant impact on everyday functioning and quality of life in children and adolescents with Autism (MacNeil, Lopes, & Minnes, 2009).

2.1.1.3 Anxiety and sleep

Sleep problems amongst the anxious, and anxiety problems amongst the sleep deprived, are well known (Cox & Olatunji, 2020). Evidence suggests that heightened and dysfunctional emotional reactivity mediates the interaction between cognitive and autonomic hyperarousal, and therefore the occurrence and maintenance of sleep problems. At the same time, emotional disturbances can be reinforced by dysfunctional sleep-wake regulating neural circuitry (Baglioni, Spiegelhalder, Lombardo, & Riemann, 2010). One cross sectional analysis of adolescents (*n*=1,014) reported that 25.6% of those with an anxiety disorder also met the criteria for insomnia, whilst a further 30.4% of those with generalised anxiety, 32.4% with social phobia, 24.3% with a specific phobia, 35.7% with a panic disorder, and 42.9% with an obsessive-compulsive disorder met the criteria for acute insomnia. An initial diagnosis of insomnia was also associated with an increased risk of later mood disorder, which suggests there is a complex and reciprocal association between anxiety and sleep (Brown et al., 2018). In another study assessing sleep problems (not insomnia), 91% of children with generalised anxiety disorder, 91% with social phobia, and 87% with obsessive-compulsive disorder displayed at least one sleep problem (Brown et al., 2018; Chase & Pincus, 2011b).

Studies have also examined causality, long term outcomes and bidirectionality between sleep and anxiety. One longitudinal study conducted by Gregory and colleagues (2005) assessed individuals at ages 5, 7 and 9, and again at age 21 and 26 (*n*=943). Those with sleep problems during childhood were significantly more likely to experience anxiety symptoms in adulthood (Gregory et al., 2005). Another longitudinal study, not assessing anxiety in particular but internalising, externalising and inferential sleep data using the CBCL, in conjunction with MRI, found that at 6 time points between the ages of 2 and 7, sleep disturbance was associated with smaller grey matter volumes and thinner dorsolateral prefrontal cortex (Kocevska et al., 2017).

2.1.2 Executive functioning

Executive functioning is an umbrella term for the set of effortful, top down processes that are responsible for goal oriented and purposeful behaviour and regulation, related to prefrontal and neocortical activity (Goldstein, Naglieri, Princiotta, & Otero, 2014). Whilst the concept of executive functioning is largely ununified and changing, with 33 current definitions, it can be broadly defined as an overarching function made up of several distinct and related processes across nine domains: attention, emotion regulation, flexibility, inhibitory control, initiation, organisation, planning, self-monitoring and working memory (Goldstein et al., 2014).

2.1.2.1 Executive functioning and Autism

Executive functioning forms part of the core cognitive profile of Autism. Planning, impulsivity, initiating activities, inhibition, working memory, shifting from one task to another or organising surroundings fall under its functional processes and are often conceptualised as deficits within Autism (Hill, 2004). In order to perform an executive functioning task, an individual must disengage from the immediate environment and guide actions or instructions that may not be immediately obvious. Executive functioning processes initiate non routine tasks, engage in flexible behaviours, remember lists of objects or instructions, and apply changes to routines; all of which are difficult tasks for individuals with Autism (Happe & Fletcher Watson, 2019). Rigidity of behaviour, the tendency to become engrossed in an activity, engaging in repetitive or elaborate rituals are conceptualised as processes absent from executive functioning. These may come to dominate the daily life of some individuals who may need prompts to initiate changes in a routine (Happe & Fletcher Watson, 2019). Children with Autism may tend to forget things or find lists of objects or instructions difficult to both remember and complete. They may appear to be disorganised but attempt to overcome this through lists or adhering to rigidity and structure. Neural damage to the frontal lobes results in atypical executive functioning, and functional differences in the prefrontal cortex are associated with other

social-emotional-behavioural-impulsivity conditions such as ADHD, Obsessive Compulsive Disorder, Tourette's Syndrome, FASD and Schizophrenia (Ozonoff & Jensen, 1999; Sergeant et al., 2002).

2.1.2.2 Executive functioning and FASD

Whilst executive functioning is often conceptualised as a central cognitive deficit of FASD, and subjective and objective executive functioning testing forms part of its diagnostic process, PAE is associated with many cognitive outcomes and there remains heterogeneity amongst the FASD executive functioning profile (Lange et al., 2017). This is most likely because of the variable nature of PAE in terms of its frequency and timing. One meta-analysis reviewing 46 studies (*n*=868) comparing FASD and TD children showed that those with FASD scored significantly higher on set shifting, working memory and inhibition processes, with set shifting scoring the highest (Khoury, Milligan, & Girard, 2015). However, executive functioning profiles in FASD are more variable than in other neurodevelopmental populations, and whilst there is a robust association between executive functioning and FASD, its profile is not as quantitatively synthesised as in Autism or ADHD (Lange et al., 2017; Nash et al., 2006). FMRI studies show that children and adolescents with FASD demonstrate activation deficiencies in in the prefrontal cortex during executive functioning tasks compared to controls (Soh et al., 2015) and there is no significant difference in executive functioning tasks across different severities of FASD (Glass & Mattson, 2017). Children with FASD show varying difficulties across the domains of planning, strategy use, attention, verbal fluency (Kodituwakku, 2009). Children with PAE also have significantly more executive functioning deficits than children with prenatal exposure to tobacco, marijuana or cocaine (Schonfeld, Paley, Frankel, & O'Connor, 2006).

2.1.2.3 Executive functioning and Sleep

Executive function changes across the lifespan. Its development is linked to the maturation of the prefrontal and connected subcortical areas that occur during typical childhood and adolescence (Diamond, 2013) and its development and decline over the lifespan tends to follow an inverted U-

shaped curve which peaks in the young adult years (Diamond, 2013). Executive functioning can be improved through training, for example through practicing working memory or cognitive flexibility tasks, however sleep is consistently found to be a mediator in improving executive functioning in both children and adults (Karbach & Unger, 2014; Vermeulen, Van der Heijden, Swaab, & Van Someren, 2019).

As mentioned in Section 1.1.4, sleep is associated with several cognitive processes which fall under the umbrella term of executive functioning. Working memory for example requires central executive control in order to operate the separate processes that contribute to its effective functioning (See Section 3.2.1 for the Working Memory Model). Periods of sleep are associated with memory consolidation in children (Ashworth et al., 2014), while spindle activity is associated with working memory and planning (Chatburn et al., 2013). Sleep quality and quantity has consistently been found to be associated with neurobehavioural functions in TD children (Kuula et al., 2015; Sadeh, Gruber, & Raviv, 2002). Experimental studies report that executive functioning performance, including verbal fluency, shifting and planning are associated with sleep loss and fragmentation (Kryger, Dement, & Roth, 2010).

As mentioned in Section 1.1.5, respiratory events such apnoea and hypopnea can be mediators of negative outcomes, some of which fall under the classification of executive functioning. Severity of sleep disturbance in obstructive sleep apnoea syndrome (OSAS) is correlated with level of executive impairment, with some residual impairment despite treatment (continuous positive airway pressure - CPAP). One meta-analysis assessing a total of 1697 TD children and adolescents, found large effect sizes for sleep and the executive functioning domain of generativity and medium effect sizes for inhibition, working memory and shifting (-0.64 to -1.06) when examining SDB and executive functioning domains (Mietchen, Bennett, Huff, Hedges, & Gale, 2016).

Studies of EEG changes throughout the course of sleep and following sleep deprivation provide further indication of the relative importance of the frontal regions of the brain to sleep (Jones 2001). In one cross sectional analysis (*n*=236) of objective sleep and executive functioning measurements (actigraphy and tower test) in TD adolescents, those with poorer sleep efficiency were significantly more likely to have poorer executive functioning scores, mediated by socioeconomic and environmental influences (Anderson 2009). One narrative review conducted by Turnbull, Reid and Morton (2013) noted a paucity of data assessing executive functioning and childhood sleep patterns, noting that only one study at that time that met their review criteria. In 2019, by contrast, a meta-analytic review assessed twenty-eight studies looking at sleep and executive functioning measurements, finding that total sleep time is related to inhibitory control attention, working memory and cognitive flexibility (Ballesio, Aquino, Kyle, Ferlazzo, & Lombardo, 2019). In the consistent functioning of the working memory, shifting and generativity processes of executive functioning, sleep is a well-documented and necessary contributor.

2.1.3 Behaviour

Healthy childhood development includes a range of social, emotional and behavioural functioning (Wenar & Kerig, 2000). Healthy social functioning involves an adequate balance between dependence on others and autonomy, and a comfortable relationship with adults and other children, with the capacity to empathise and share. Healthy emotional functioning involves an adequate degree of emotional stability, capacity for self-assessment, a tolerance for frustration and ability to cope with conflicting emotions, whilst healthy behavioural functioning in children requires flexibility in behaviour, integrative capacity, mastery, self-concept and awareness (Wilks, Gerber, & Erdie-Lalena, 2010). Behavioural difficulties are a normal part of development; for example, it is accepted that typically developing young children can be restless, hyperactive, overactive, oppositional and defiant, anti-social or may not grasp social cues, even though these traits and characteristics contribute to the diagnostic criteria of several neurodevelopmental conditions. Furthermore, typical development

usually includes changing phases of temperament, such as increased irritability, issues with attachment, aggression or withdrawal. When addressed successfully by caregivers, these should decrease as the child moves to the next stage of development (Wenar & Kerig, 2014). However, neurodevelopmental conditions relating to behaviour occur when (irrespective of the neuromechanics or environmental situations involved) certain patterns of entrenched behaviour form a psychopathology. Periods of maladjustment following an identified stressor can be identified in attentional disorders such as ADHD, oppositional defiance disorder, Autism, disorders of anxiety and depression, bipolar disorders, conduct disorders and Fetal Alcohol Spectrum Disorders.

2.1.3.1 FASD and behaviour

The Neurobehavioural Screening Test is a widely used tool to differentiate or screen for children with FASD. It was comprised of factor analysis of the CBCL through the identification of the most common areas of behavioural difficulty. These are:

Behaviours that are younger than age related expectations. Children with FASD will often reach developmental milestones in early childhood, after which both cognitive and social behaviours tend to plateau (Catterick & Curran, 2014). This results in inabilities to comprehend concepts such as social reciprocity or emotional awareness which means that children with FASD tend to exhibit behavioural immaturity.

Oppositional defiance; disorders of conduct. Ninety percent of children with FAS have a diagnosis of conduct disorder, a precursor to antisocial behaviour disorder (Popova, Lange, Shield, et al., 2016). This may explain the large numbers of individuals with FASD seen in the criminal justice system and is the result of atypical fear-empathy responses related to distress, as well as problems with the understanding of normative social concepts (Bower et al., 2018).

Lying, cheating. In educational settings, children with FASD are often described as having the ability to lie or cheat in order to answer questions or evade situations, but not understand the consequences or moral concept of lying. The lie-telling abilities of children aged between 4-8 years with FASD were examined in one study by Rasmussen and colleagues (2008) using a temptation-resistance paradigm, in which a significantly higher number of FASD than TD children (94% verses 72%) lied about secretly looking at a toy (Rasmussen, Talwar, Loomes, & Andrew, 2008). This was conceptualised as the result of a lack of inhibitory control combined with not understanding the consequences of actions (Taylor et al., 1999). Children with FASD often confabulate stories in order to answer questions which they cannot remember the answer to, due to attentional or memory problems, or can lack moral maturity (Novick Brown et al., 2012; Schonfeld, Mattson, & Riley, 2005).

Lacking guilt after misbehaving/ acts of cruelty/ stealing. In TD children, a lack of remorse after misbehaving is an indication of a lack of empathy, rationalising actions in an unsociable way, or blaming others for an individual's actions (Wenar & Kerig, 2000). In children with FASD, a lack of guilt after misbehaving is the result of not understanding the social concept of expected behaviours. Concepts of justice or ownership are often alien to a child with FASD and can result in cruelty or stealing behaviours (Brown, 2015).

Attentional problems, impulsivity and hyperactivity. Attentional problems result in the most visible behaviours in children with FASD, namely atypical levels of inhibition, compulsion, distractibility and attention span (Peadon, Fremantle, Bower, & Elliott, 2008). Indeed, ADHD like symptoms are part of its pathognomonic features (Kingdon, Cardoso, & McGrath, 2016). There is a significant overlap between ADHD and FASD, and ADHD is prevalent in between 30-50% of children with FASD (Peadon, 2010). There is some evidence that ADHD in FASD may be a specific clinical subtype and may require an alternative treatment approach.

2.1.3.2 Autism and behaviour

As a pervasive developmental condition, Autism results in a wide range of atypical behaviours, mainly around social interaction and understanding social nuances. Although there is some contention as to the process of delineating specific Autism behaviours (Happe & Fletcher Watson, 2019), as with FASD, the CBCL is a widely used tool in the factor analysis of Autism specific behaviours (Hanratty et al., 2015). Children and adults with Autism tend to score highly in the subsets of social behaviour, thought behaviour, attention behaviour, withdrawn, and aggressive behaviour when using the CBCL or its adult counterpart, the Adult Behaviour Checklist (ABCL). Scores tend to be more internalised than externalised, but there is a heterogeneity within the Autism profile outside of the behaviours pertinent to its diagnosis (Havdahl, von Tetzchner, Huerta, Lord, & Bishop, 2016; Mazefsky, Anderson, Conner, & Minshew, 2011; Ooi, Rescorla, Ang, Woo, & Fung, 2011).

2.1.3.3 Sleep and behaviour

Persistent sleep disruptions can have long term negative neurodevelopmental consequences, or a negative effect on neuropsychological functioning. Cognitive performance underlies behavioural output, can be mediated by sleep, and can contribute to the behavioural manifestations seen in neurodevelopmental conditions (Kamara & Beauchaine, 2019). This includes difficulty in cognitive performance, learning, as well as difficulties with new and abstract concepts (Hill et al., 2007), behaviour and attention (Sadeh et al., 2002; Shang, Gau, & Soong, 2006). Sleep deprivation for example in teenagers has a negative impact on emotional and behavioural problems as well as an alteration in attention and performance (Dahl, 1999). Similarly, there is a relationship between quality of sleep, impulsive behaviours and hyperactivity (Giannotti, Cortesi, Sebastiani, & Ottaviano, 2002; Spruyt & Gozal, 2011b).

One meta-analysis conducted by Astill and colleagues in 2012 assessing sleep, cognition and behavioural problems in school-aged children aged between 5 and 12 years (*n*=35,936) found that shorter sleep duration was significantly related to internalising (r=0.09,CI[0.06,0.12]) and externalising (r = .08, CI [.06, .11]) behavioural problems (Astill, Van der Heijden, Van Ijzendoorn, & Van Someren, 2012). In one systematic review assessing sleep in relation to cognition and behaviour in preschool and school aged children, Reynaud and colleagues (2018) found that in 12 out of 13 studies that met quality criteria (low risk of bias, high sample size, cross sectional design, assessment of confounding factors, objective measurements) higher quantity and quality of sleep was related to better behavioural outcomes (Reynaud et al., 2018). One article in this study extended its participant criteria to 9 years (Armstrong, Ruttle, Klein, Essex, & Benca, 2014) whilst the other 12 were related only to preschool aged children. Insomnia and parasomnias in school aged children was positively associated with aggressive behaviour, attentional problems and externalising behaviour (Reynaud et al., 2018). One longitudinal study conducted by Muratori et al. (2019) found that in their sample of children aged 6 to 10 years (*n*=227), an association was found between an increase in sleep problems and the worsening of behavioural problems (inattention and hyperactivity), however no association was seen with conduct problems (Muratori et al., 2019).

2.1.4 Summary

Anxiety, executive functioning and behavioural problems are prevalent in both FASD and Autism. There are some distinctions and some similarities between the FASD and Autism profile, as well as contentions regarding the methodological validity of the measurement of anxiety and behaviour in both groups. Both children with FASD and Autism tend to experience clinical levels of anxiety, which can manifest differently according to syndrome and differ according to environmental influences on worries and fears. Children with FASD tend to experience more 'worry' based anxieties whilst children with Autism tend to experience more 'fear' based anxieties. Both children with FASD and Autism tend to score above clinical ranges in executive functioning, however whilst the executive functioning

profile is well characterised in the Autism population, it is more heterogenous in the FASD population due to the variability of PAE. Children with Autism tend to score heterogeneously on externalised/ internalised behaviour profiles whereas children with FASD tend to present with more oppositional and defiant behaviours.

Sleep is strongly associated with the emotion behaviour, and executive control triad, but this relationship is less well understood in atypical populations. With this in mind, Study 1 of this thesis aimed to test and investigate these associations.

2.2 Aims and hypotheses

The aims of this study are:

1. To describe caregiver reported sleep habits, anxiety, executive functioning and behaviour in FASD, Autism and TD groups.
2. To examine whether sleep habits, anxiety, executive functioning and behaviour are 'syndrome specific', i.e. are statistically different than the other two groups.
3. To investigate whether sleep habits as measured by the CSHQ predict the variance in executive functioning, behaviour or anxiety in TD children, and children with FASD or Autism.
4. To investigate whether the strength of the association between sleep problems or sleep behaviours is dependent on age, sex or socioeconomic status of the child.

It is predicted that:

1. Children with FASD and Autism will present with higher scores in the BRIEF, SCAS and CBCL than TD children. (Kodituwakku, 2009, Lange 2017).

2 . a) Children with FASD will present with a higher number of attentional and conduct problems than TD or children with Autism (Popova, Lange, Shield, et al., 2016).

b) Children with Autism will present with a higher number of social and communication difficulties than children with FASD (Stevens et al., 2013).

c) Children with FASD and Autism will present with a higher number of sleep problems than TD children (Inkelis & Thomas, 2018; Mazzone et al., 2018).

3. Sleep habits will be significantly correlated with executive functioning, behaviour and anxiety in the three groups. (Cohen, Conduit, Lockley, Rajaratnam, & Cornish, 2014; Gregory & Sadeh, 2012; Wengel, Hanlon-Dearman, & Fjeldsted, 2011).

4. a) There will be higher anxiety scores amongst girls than boys in all three groups. (Buckhalt et al., 2007; Kodituwakku, 2009)

   b) There will be higher maladaptive behaviour scores amongst boys than girls in all three groups (Buckhalt et al., 2007; Kodituwakku, 2009; Mukherjee, Wray, Commers, Hollins, & Curfs, 2013; Werling & Geschwind, 2013)

   c) Age will predict severity of sleep disturbances, maladaptive behaviour and anxiety in the three groups. (Buckhalt et al., 2007; Kodituwakku, 2009; Mukherjee, Wray, Commers, Hollins, & Curfs, 2013)

   d) SES will be a predictor of sleep, behaviour and anxiety in the three groups (Buckhalt et al., 2007; Kodituwakku, 2009; Mukherjee, Wray, Commers, Hollins, & Curfs, 2013; Werling & Geschwind, 2013).

2.3 Power Analysis

A priori and post hoc power analyses were conducted in SPSS to ascertain sample sizes. The purpose of this thesis is to examine whether sleep is a contributor to anxiety, behaviour and executive functioning. As there are no null hypotheses, the power analysis conducted here includes 12 variables (8 CSHQ subscales and 3 covariates). This yielded a sample size of 40 in each group for power of 0.8. A larger sample would yield >0.8. Table 2.1 outlines the a-priori power analysis, whilst post hoc analyses are outlined in Section 2.5.

Table 2.1: A-Priori power analysis to determine sample size for Study 1

F tests - Linear multiple regression: Fixed model, R^2 increase	
Effect size f^2	0.5
α err prob	0.05
Power (1-β err prob)	0.8
Number of tested predictors	8
Total number of predictors	11
Noncentrality parameter λ	*20*
Critical F	*2.29*
Numerator df	*8*
Denominator df	*28*
Total sample size	***40***
Actual power	0.81

2.4 Methodology

2.4.1 Ethical approval

This study was approved by the UCL Institute of Education Research Ethics Committee (Approval number 16683/001). All caregivers were provided with details of the study, and details on what will happen with the information they provide. All caregiver participants gave written informed consent (See Appendix).

2.4.2 Materials

This study used several questionnaires to assess parentally reported sleep and daytime functioning, as well as relevant background information.

Children's Sleep Habits Questionnaire (CSHQ; Owens et al., 2000; described in Section 1.1.7.1.1) This is a 33 item retrospective parent report which screens for common sleep problems for school aged children. Parents indicate the frequency of various sleep related characteristics, using a Likert Scale with three options: 'rarely' for an event that occurs 0-1 times per week; 'sometimes' for an event that occurs 2-4 times per week; 'usually' for an event that that occurs between 5-7 times per week. Questions include occurrences of problems around bedtime routines, indications that the child is not

sleeping a normal amount, or indications that the child is waking during the night. Items are grouped into eight subscales: Bedtime Resistance, Sleep Onset Delay, Sleep Duration, Sleep Anxiety, Night Waking, Parasomnia, Sleep Disordered Breathing, Daytime Sleepiness. The CSHQ is a widely used assessment tool in paediatric sleep, with high internal validity and Cronbach Alpha score of 0.83. Clinical scores are determined as 41 or above (Markovich, Gendron, & Corkum, 2015).

Spence Children's Anxiety Scale (SCAS; Spence, 1997; Spence, 1998): This is a 38-item questionnaire measuring anxiety symptoms in children aged between 6-16, used in the measurement of symptoms of DSM-V anxiety disorders, in both mainstream and non- mainstream settings. It includes subscales for Separation Anxiety, Social Phobia, Obsessive-Compulsive Disorder, Panic, Physical Injury Fears and Generalised Anxiety Disorder. Each item is on a 4-point Likert Scale ranging Never (0), Sometimes (1) Often (2) Always (3). The SCAS has high internal validity with a Cronbach's Alpha score of 0.92 (Essau, Muris, & Ederer, 2002). Clinical scores are determined as 31 and above.

The Behavior Rating Inventory of Executive Function (BRIEF; Roth, Isquith, & Gioia, 2014): This is an 83 item parental report outlining the six subsets of executive functioning based on a three point Likert Scale, Never (1), Sometimes (2), Often (3). Subsets include Working Memory, Inhibition, Shifting, Emotional Control, and Planning and Organisation. The BRIEF is a widely used instrument for executive functioning with high internal validity and internal consistency, Cronbach's Alpha score of 0.8-0.98 (Roth et al., 2014). Clinical scores are determined as 65 and above.

Child Behavior Checklist/ Achenbach System of Empirically Based Assessment (CBCL; (Achenbach & Rescorla, 2003)*: A* widely used tool for the measurement of maladaptive behaviours and emotional problems in children, consisting of 118 questions on a three-point Likert Scale: 'not true (0)'; 'somewhat true (1); 'very true (2). Subscales are divided into 'Internalising' and 'Externalising' behaviours as well as the Subsets of: Withdrawn, Somatic Complaints, Anxious/ Depressed, Social Problems, Thought Problems, Attention Problems, Delinquency and Aggression. Although the CBCL is

designed to report on the parental observations of emotional and behavioural problems of their own children, it has been used in research settings with other significant adults, such as mental health workers, hospital staff, foster parents, clinicians, and teachers. It has high internal validity, with a 0.94 Cronbach's Alpha score. Clinical scores are determined as a total of 64 and above (Bean, Mooijart, Eurelings-Bontekoe, & Spinhoven, 2006).

The Childhood Autism Rating Scale, Parents Version (CARS; Lord & Schopler, 1987). This is a 15 item screening questionnaire that determines the severity of Autism symptoms, using a seven point (including midpoint) Likert Scale, ranging from typical to atypical behaviour. Categories are: relating to people, imitation, emotional responsiveness, body use, object use, adaptation to change, visual responses, listening responses, taste, smell, touch responses, fear or nervousness, verbal communication, nonverbal communication, activity levels, intellectual responsiveness and general observations. The CARS demonstrates moderate to good sensitivity and specificity (81.4% and 78.6% respectively) and good internal consistency (Cronbach's Alpha =0.79) however cannot be used in place of a diagnostic assessment. A CARS score of >=33 indicates possible Autism (Garfin & McCallon, 1988).

Neurobehavioural Screening Tool (NST; Kelly Nash, Koren, & Rovet, 2011). This is a ten-item binary checklist that screens for possible FASD in children. Questions examine whether children meet the more common neurobehavioural characteristics of FASD, however these are not always accurate or representative of all children with FASD. Categories are: acting young, lying and cheating, lacking guilt after misbehaving, difficulty concentrating, impulsivity, hyperactivity, displays of cruelty, stealing at home, and stealing outside of home. The NST has low sensitivity but high specificity (62% and 100% respectively) and in the absence of a more accurate measurement tool, is a widely used screening mechanism for FASD in children. Scores above 8, plus confirmed prenatal alcohol exposure indicate a FASD diagnostic evaluation should be carried out (Kelly et al., 2011).

Socioeconomic (SES) questionnaire. Caregivers were asked their ethnic origin, educational qualifications and job titles of all adults in the household, the number of parents in the household, and whether the child was in foster care, adoptive care, or under the care of a biological parent or relative. SES was determined along the National Statistics Socio-economic Classification of 1 (higher or lower managerial, administrative or professional occupations and higher education), 2 (intermediate occupations and A-Levels or equivalent), or 3 (routine or manual occupations or unemployed, some schooling) (Office for National Statistics, 2016).

2.4.3 Statistical analysis

Data were analysed using the haven, glmnet and xtable packages in R, as well as IBM Statistical Package for Social Science V.22. Outlying scores were identified through Cook's distances and removed. Analyses where the significance of results changed once outliers were removed are labelled as 'OR' (Outliers Removed).

2.4.3.1 Group comparisons

Raw scores on the CSHQ, CBCL, SCAS and BRIEF were compared using one-way between-group Analysis of Variance (ANOVA) to compare the FASD, Autism and TD groups. Data were examined for normality using Levene's Test of homogeneity. In post-hoc analysis where equal variances could not be assumed, the Games-Howell test was used. Where equal variances were assumed, the Bonferroni Correction was used (Field, 2018). Raw scores were used since T-scores are capped and often exceeded in these clinical groups.

To determine whether sex was a confounding factor, independent samples t-tests were used to compare males and females within each group. Pearson's correlations were used to investigate age-related changes in sleep, executive function, anxiety and behaviour. One-way ANOVAs were used to determine whether SES differences contributed to either sleep or psychological outcomes, per group.

Since some age, SES and sex differences were found, all subsequent analyses were conducted using age, SES and sex as covariates.

2.4.3.2 Regression analysis

Pearson correlations were carried out on the subscales of all questionnaires to check for multi collinearity. Tolerance Statistics of >0.9 were searched for, none were found. Where any correlations were above 0.8, these were removed from multiple regression analyses and assessed separately. Hierarchical multiple linear regression using the Enter model was used to assess whether sleep was able to predict either the total or subscales of executive function, anxiety, or behaviour in Autism, FASD or TD groups. Block one always controlled for age, SES and sex. Composite CSHQ subscale scores were taken together as a representation of sleep disturbance and were entered in Block two. Total scores were not used since the CSHQ counts scores on two subscales twice. Separate models were run assessing Total CSHQ vs Total BRIEF/ SCAS/ CBCL. Separate models were run for each subscale and Total of the BRIEF, SCAS and CBCL. Adjusted R^2 values are reported as the percentage of variance, in order to control for the number of predictors in the model.

2.4.3.3 Test of similarity (rather than difference)

It is possible to show that results between the two groups are statistically different by comparing values in a T-Test. In children with FASD and Autism, there appear to be several similarities as well as differences and in order to ascertain which domains were syndrome specific, or which domains overlapped between syndromes, significant similarities were calculated using Two-One-Sided Tests of Similarity (TOST). Glmnet, xtable, and haven packages were used to import, manipulate and report data in R and conduct TOST's.

2.4.4 Participants

Participants were caregivers of children aged between 6 and 15 years (between the 6th and 16th birthday). This age group was chosen since it represents a large age range from which a cross sectional analysis could be made.

All children had received either a diagnosis of FASD, Autism, or had no diagnoses. Screening tools for FASD and Autism were additionally included in the battery of questionnaires that caregivers completed. A number of children also had secondary diagnoses, which are outlined in Table 2.1 below.

This study was initially advertised as an online questionnaire assessing sleep and daytime functioning in children with FASD or Autism. Caregivers of TD participants were recruited through three schools in West London, South London, and Milton Keynes. Caregivers of children with FASD were recruited through the UK FASD Network mailing list, while caregivers of children with Autism were recruited through online Autism forums. Caregivers were directed to an online questionnaire, at the end of which there was an option to receive feedback on the child's score, as well as sleep hygiene intervention ideas (See Appendix for sample feedback booklets and recruitment material).

A total of 322 caregivers completed the online questionnaire. Nine were excluded as they had not completed large sections of the questionnaire. Twenty-four were excluded as they did not have a diagnosis of FASD or Autism, and were not TD. A further 10 were excluded as they did not meet the age criteria. One- way between group ANOVAs indicated no age ($F(1,235)=1.06$, $p=0.43$, $\eta_p^2=0.85$) or SES differences ($F(1,3)=1.06$, $p=0.49$, $\eta_p^2=0.01$) but there were significant differences between sex, with significantly more boys than girls ($F(1,2)=6.58$, $p=0.01$, $\eta_p^2=0.02$). The final sample consisted of 279 participants, outlined in Table 2.1.

Table 2.2: Participant details

	Autism	FASD	TD
n	61	114	104
Male/Female	46/15	62/51	55/48
Age (M(SD))	10.03(2.54)	9.54(2.86)	9.43(2.55)
Age Range	6.07-15.56	6.09-15.98	6.47-15.90
SES 1/2/3	17/35/9	14/74/26	23/67/15

Participants filled in an online form created in Typeform. This platform was used as it proved an effective way of both recruiting and maintaining that the participant continued all the way through the questionnaire and had the additional option of leaving the questionnaire and coming back to it later. It was also available for use on mobile phones which made it more accessible. Participants were informed at the beginning that they were welcome to leave the study by not filling in the questionnaire, but if they wanted full and accurate feedback of their child's CSHQ, SCAS, CBCL and BRIEF scores it was necessary to fill in all questions. Additionally, the participant was prompted once if a question was missed, and thereafter given the option to leave. As a result, there was 92% response rate with 146 missing values. Where there were missing data, these were imputed in SPSS.

2.5 Results

2.5.1 Power

Post hoc statistical power analyses were carried out to find the probability of whether significant findings were truly significant, given the possibility of committing Type I or Type II error. This informs us of the probability of significant associations in the present samples being likely to appear in the population. Conventionally a power score of 70% (0.7) or above indicates a good probability, and scores of 0.8 and above indicate a strong probability (Field, 2018).

Throughout the results section, statistical significance is reported using *p* values, where $p<0.05$ and $p<0.001$ are reported as significant and highly significant. Effect sizes are reported using significant (p=<0.05) R^2 values and ηp^2 depending on whether the data was regression (R^2) or group comparison (ηp2). Meanwhile, the power of significant (p=<0.05) R^2 values are reported using F ratios, which report the ratio of the proportion of variance accounted for versus the proportion of variance unaccounted for. It is used here to describe the fit of the data, as reported by Fraley & Vazire (2014). This allows for the interpretation of whether the data reported here, with the sample sizes reported, can predict the fit of the sample data to the population. Meanwhile, the table below sets out an overview of post hoc power analyses that were conducted, related to each of the hypotheses. The implications of these are discussed further in the limitations and discussion sections.

Table 2.3: Post Hoc Power Analysis for Study 1.

	Noncentrality Parameter λ	Critical F	Power 1-B error
Hypothesis 1, Group comparisons: Sleep	18.8	3.02	0.98
Hypothesis 1, Group comparisons: Anxiety	4.71	3.88	0.68
Hypothesis 1, Group comparisons: Behaviour	34.18	3.88	0.99
Hypothesis 1, Group comparisons: Executive Function	49.22	3.87	0.99
	Noncentality Parameter δ	Critical t	Power
Hypothesis 2, ASC>FASD Social Communication	2.61	1.97	0.74
Hypothesis 2b Clinical>TD Sleep Problems	2.65	1.97	0.77
Hypothesis 3 Regressions/CSHQ	Noncentrality Parameter λ	Critical F	Power
ASC / SCAS	16.56	3.14	0.95
ASC / CBCL	13.85	3.16	0.91
ASC / BRIEF	35.34	2.44	1.00
FASD / SCAS	31.12	3.08	1.00
FASD / CBCL	35.34	2.44	1.00
FASD / BRIEF	37.80	2.44	1.00
TD / SCAS	21.94	3.09	0.99
TD / CBCL	18.06	3.16	0.97
TD / BRIEF	36.36	2.45	1.00
Hypothesis 4, Age/Score	Noncentrality Parameter λ	Critical F	Power
ASC / SCAS	0.75	3.15	0.11
ASC / CBCL	4.76	3.15	0.46
ASC / BRIEF	3.26	3.15	0.33
ASC / CSHQ	1.36	3.15	0.16
FASD / SCAS	1.60	3.08	0.18
FASD / CBCL	7.98	3.08	0.70
FASD / BRIEF	7.98	3.08	0.70
FASD / CSHQ	8.32	3.09	0.72
TD / SCAS	4.16	3.09	0.42
TD / CBCL	7.98	2.44	0.79
TD / BRIEF	9.36	3.09	0.77
TD / CSHQ	5.70	3.08	0.55
Hypothesis 4, SEX/Score	Noncentality Parameter δ	Critical t	Power
ASC / SCAS	4.23	1.97	0.99
ASC / CBCL	0.80	1.98	0.12
ASC / BRIEF	3.05	1.99	0.86
ASC / CSHQ	4.42	1.99	0.99
FASD / SCAS	5.06	1.98	1.00
FASD / CBCL	4.97	1.98	1.00
FASD / BRIEF	0.99	1.98	0.17
FASD / CSHQ	1.93	1.98	0.48
TD / SCAS	4.77	1.98	1.00
TD / CBCL	4.62	1.98	1.00
TD / BRIEF	2.98	1.98	0.84
TD / CSHQ	4.04	1.98	0.98
Hypothesis 4, SES/Score	Noncentality Parameter δ	Critical t	Power
ASC / SCAS	1.36	3.14	0.16
ASC / CBCL	1.15	3.08	0.14
ASC / BRIEF	1.35	3.09	0.16
ASC / CSHQ	1.12	2.69	0.12
FASD / SCAS	2.51	3.08	0.27
FASD / CBCL	4.60	3.08	0.46
FASD / BRIEF	3.42	3.08	0.35
FASD / CSHQ	4.16	2.70	0.36
TD / SCAS	2.30	3.08	0.25
TD / CBCL	5.60	2.69	0.47
TD / BRIEF	1.48	3.08	0.17
TD / CSHQ	5.75	3.08	0.55

2.5.2 CSHQ

The CSHQ variables were analysed using group mean comparisons. Effect sizes are displayed as partial eta squared (η_p^2). Effect sizes are calculated as small (between 0.10 and 0.30), medium (between 0.30 and 0.50) and large (>0.50) according to Cohen (2013). ANOVA results are presented in Table 2.4. Following this, group comparison, raw score, SES, sex and age differences for each CSHQ subscale are set out below.

Table 2.4: Mean scores (SD) and group differences using ANOVA for CSHQ subsets

	Autism (n=61)		FASD (n=114)		TD (n=104)		F	p	ηp2
	M	SD	M	SD	M	SD			
Bedtime Resistance	9.66	3.35	9.67	3.39	8.81	3.03	2.25	0.11	0.17
Sleep Onset Delay	2.24	0.78	2.40	0.71	1.73	0.79	21.82	<0.001	0.14
Sleep Duration	5.20	1.69	5.62	1.93	4.29	1.59	15.58	<0.001	0.11
Sleep Anxiety	7.56	2.85	7.75	2.97	6.23	2.32	9.23	<0.001	0.07
Night Wakings	5.29	1.88	5.72	1.83	4.20	1.24	23.50	<0.001	0.15
Parasomnias	11.76	3.64	12.89	3.82	9.97	2.96	18.80	<0.001	0.12
Sleep Disordered Breathing	4.34	2.03	4.27	1.88	3.83	1.41	2.32	0.10	0.02
Daytime Sleepiness	12.34	3.72	13.51	3.16	10.94	3.61	14.54	<0.001	0.10
Total CSHQ	54.85	10.62	58.63	11.00	40.18	9.27	46.85	<0.001	0.26

2.5.2.1 Bedtime Resistance

Raw Score: Overall, the tests of between subject effects on Bedtime Resistance showed no significant differences. In post-hoc analysis and tests of similarity, there were no significant differences between the TD/ Autism or TD/FASD, but there were significant similarities between the Autism/ FASD groups when using the range of acceptability of 10% (*p*=0.001).

SES/Sex: There were no significant SES or sex differences in Bedtime Resistance in in the Autism, FASD or TD groups.

Age: There were significant age differences in Bedtime Resistance in the FASD scores with older children presenting with higher levels of bedtime resistance ($F_{(1,105)}$=4.71, p=0.03, R^2=0.10), indicating that age is a predictor of bedtime resistance in the FASD but not Autism or TD groups.

2.5.2.2 Sleep Onset Delay

Raw Score: Overall, the tests of between subjects effects on Sleep Onset Delay showed significant differences between the three group means, with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=21.82, p=<0.001, R^2=0.14). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD (p=<0.001; FASD group scoring higher) groups, but no significant similarity (or difference) between the Autism/ FASD groups.

SES: There were no significant overall SES differences in Sleep Onset Delay in in the FASD or TD groups. However in the Autism group, there were significant differences between the SES groups 1 and 3, with the lower SES group scoring higher than the higher SES group ($F_{(2, 55)}$=4.78, p=0.012, R^2=0.15).

Sex and age were not significant predictors of Sleep Onset Delay in any of the groups.

2.5.2.3 Sleep Duration

Raw Score: Overall, the tests of between subjects effects on Sleep Duration showed significant differences between the three groups with clinical groups showing lower sleep duration than the TD group ($F_{(2, 267)}$=15.58, p=<0.001, R^2=0.11). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=0.004; Autism group showing lower sleep duration levels) and TD/FASD (p=<0.001; FASD group showing lower sleep duration levels) groups, but no significant similarity (or difference) between the Autism/ FASD groups.

Age: There were significant age differences in Sleep Duration in the TD scores with younger children sleeping longer than older children ($F_{(1, 102)}$=3.46, p=0.05, R^2=0.11), indicating that age is a predictor of sleep duration in the TD but not FASD or Autism groups. Sex and SES were not predictors of Sleep Duration in any of the groups.

2.5.2.4 Sleep Anxiety

Raw Score: Overall, the tests of between subjects effects on Sleep Anxiety showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 267)}$=9.23, p=<0.001, R^2=0.07). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=0.01; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher). There was significant similarity between the Autism/ FASD groups when using the range of acceptability of 10% (p=0.01).

Age: There were significant age differences in Sleep Anxiety in the FASD scores with older children showing higher levels of sleep anxiety than younger children ($F_{(1, 106)}$=3.99, p=0.05, R^2=0.04), indicating that age is a predictor of sleep anxiety in the FASD but not Autism or TD groups.

Sex and SES were not predictors of Sleep Anxiety in any of the groups.

2.5.2.5 Night Waking

Raw Score: Overall, the tests of between subjects effects on Sleep Anxiety showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 267)}$=23.50, p=<0.001, R^2=0.15). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher), but no significant similarity (or difference) between the Autism/ FASD groups.

Sex, age and SES were not significant predictors of Night Waking in any of the groups.

2.5.2.6 Parasomnia

Raw Score: Overall, the tests of between subjects effects on Parasomnia showed significant differences between the three groups with clinical groups scoring higher than TD ($F_{(2, 267)}$=18.80, p=<0.001, R^2=0.12). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=0.005; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher) but no significant similarity (or difference) between the Autism/ FASD groups. Sex, age and SES were not significant predictors of Parasomnia in any of the groups.

2.5.2.7 Sleep Disordered Breathing (SDB)

Raw Score: Overall, the tests of between subject effects on SDB showed no significant differences between the three groups. In post-hoc analysis and tests of similarity, there were no significant differences or similarities in raw scores between the TD/ Autism and TD/FASD groups. Sex, age and SES were not significant predictors of SDB in any of the groups.

2.5.2.8 Daytime Sleepiness

Raw Score: Overall, the tests of between subject effects on Daytime Sleepiness showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 267)}$=14.54, p=<0.001, R^2=0.10). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=0.037; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher) but no significant similarity between the Autism/ FASD groups.

SES: There were no significant overall SES differences in Daytime Sleepiness in in the Autism or FASD groups, however in the TD group, daytime sleepiness was associated with SES ($F_{(2, 101)}$=7.015, p=0.001, R^2=0.12). Post-hoc analysis showed that SES differences were significant between SES statuses 1 and 3, with the lower SES group showing more daytime sleepiness than the higher SES group. This indicates that daytime sleepiness levels in TD children from lower SES are higher than those of TD children from higher SES.

Sex: There were no significant sex differences in Daytime Sleepiness in the Autism, FASD or TD groups.

Age: There were significant age differences in Daytime Sleepiness in the TD scores with older children scoring higher than younger children ($F_{(1, 104)}$=18.72, p=<0.001, R^2=0.16), indicating that age is a predictor of daytime sleepiness in the TD but not for Autism or FASD groups.

2.5.2.9 CSHQ Total

Raw Score: Overall, the tests of between subject effects on CSHQ Total scores showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 267)}$=4.85, p=<0.001, R^2=0.26). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher) but no significant similarities were found.

SES/ sex: There were no significant overall SES and sex differences in CSHQ Total in in the Autism, FASD or TD groups.

Age: There were significant age differences in CSHQ total for the TD group, with older children scoring higher than younger children ($F_{(1, 102)}$=4.89, p=0.03, R^2=0.05) indicating that age is a predictor of sleep problems in the TD group but not the Autism or FASD groups.

2.5.3 CSHQ summary

According to parental report, children with Autism and FASD scored significantly higher than TD children in the subscales of sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, daytime sleepiness and CSHQ total. Scores were also higher for the clinical groups on the two remaining subscales, bedtime resistance and SDB but with smaller effect sizes (See Figure 2.1) Children with Autism and FASD had significantly similar scores in the areas of bedtime resistance and sleep anxiety. There were a number of age-attributable changes seen in the TD and FASD groups, but not the Autism group. Age was a significant predictor of bedtime resistance and sleep anxiety in the FASD group, and sleep duration, daytime sleepiness, and total CSHQ score in the TD group. Age was not a significant predictor of CSHQ scores in the Autism group. SES predicted sleep onset delay in the Autism group, and daytime sleepiness in the TD group. There were no sex differences in CSHQ scores in any of the groups. Age was a significant predictor of bedtime resistance and sleep anxiety in the FASD group, and sleep duration, daytime sleepiness, and total CSHQ score in the TD group. Age was not a significant predictor of CSHQ scores in the Autism group.

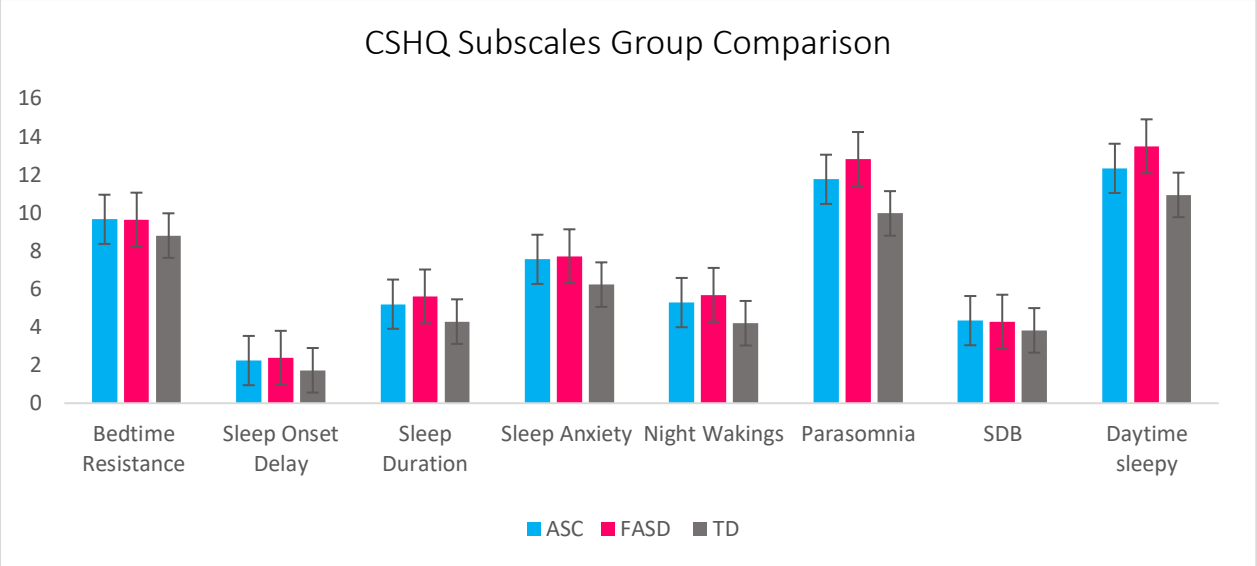


Figure 2.1: CSHQ: Comparison between Autism, FASD and TD scores on the CSHQ subscales (SE bars).

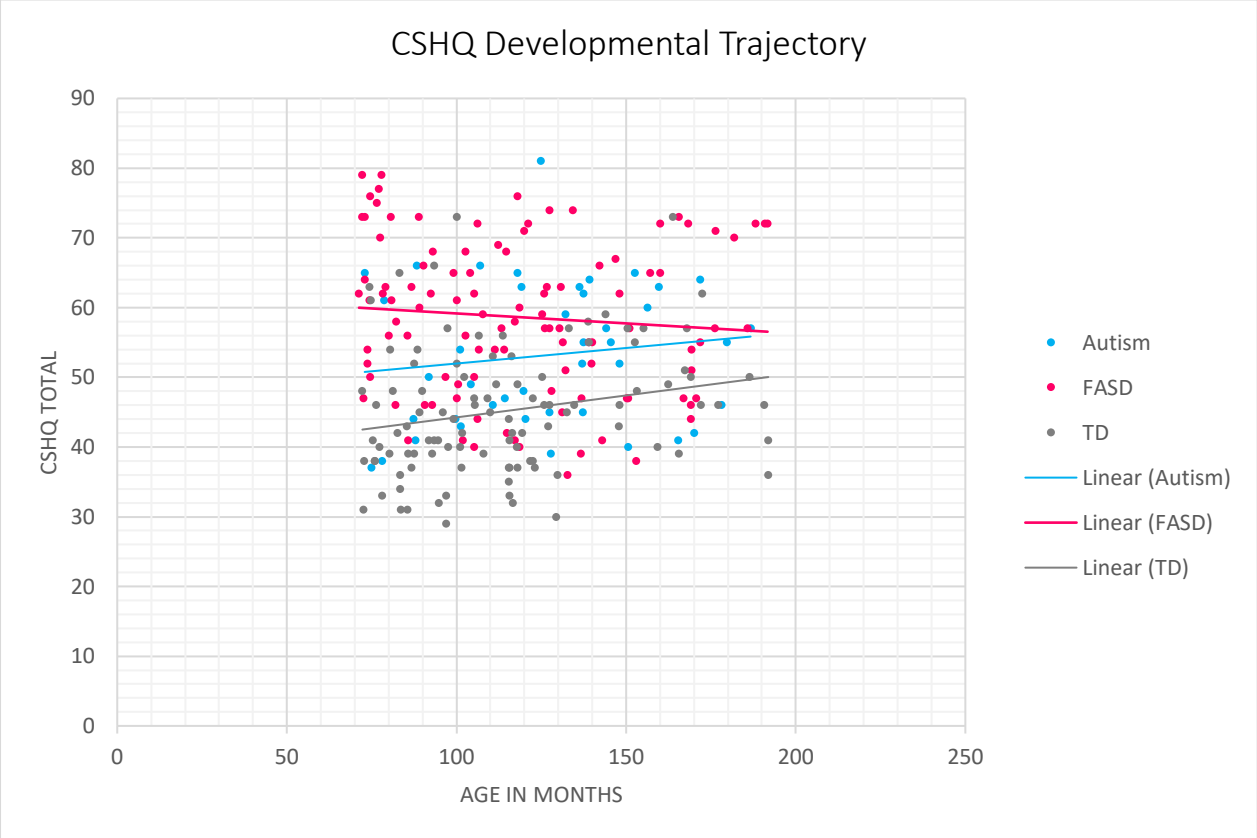


Figure 2.2: Developmental trajectory scatter plot showing CSHQ total against age in the three groups. Results are not significant but slight trends can be seen anyway.

To lay out the results in the most comprehensive way, the following sections of this chapter are comprised of separate reports for each subscale of the SCAS, BRIEF and CBCL, each beginning with a short introduction. The purpose of this is to report all significant (as well as non-significant) findings in order to investigate to which extent bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, sleep disordered breathing, daytime sleepiness, total CSHQ contribute to each psychometric variable. This can then inform a more comprehensive discussion to follow later.

2.6 Results: The Spence Children's Anxiety Scale (SCAS)

The purpose of the following section is to report anxiety scores for the three samples, compare scores between and within the groups, and infer whether sleep disturbances contribute to anxiety in the three groups. This is bearing in mind that anxieties are an intrinsic part of both Autism and FASD; children with FASD tend to experience higher rates of social and separation anxiety, whilst children with Autism tend to experience higher rates of obsessive or panic related anxieties (e.g. Popova et al., 2016). Anxiety is likely to interfere with the process of getting to sleep, as well as have an effect on its function, but at the same time, anxiety increases when an individual is deprived of sleep. The following section should be interpreted with this bidirectionality and intrinsicality in mind.

The SCAS variables were analysed using group mean comparisons and effect sizes are displayed as partial eta squared (η_p^2), presented in Table 2.5. Hierarchical multiple regression analyses were conducted in order to examine the associations between each SCAS subscale and CSHQ subscale. These are presented in Tables 2.6 -2.12

Table 2.5: Mean scores (SD) and group differences using ANOVA for SCAS subsets

	Autism (n=61)		FASD (n=114)		TD (n=104)		F	p	ηp2
	M	SD	M	SD	M	SD			
Panic	5.78	5.20	6.14	4.50	2.00	2.88	30.24	<0.001	0.19
Separation Anxiety	7.90	4.40	8.22	4.65	5.36	4.63	11.56	<0.001	0.08
Physical Injury	5.55	3.31	5.56	3.18	4.58	3.27	2.92	0.06	0.02
Social Phobia	7.62	4.34	8.66	4.58	6.21	4.42	7.98	<0.001	0.06
Obsessive Compulsive	5.14	3.77	4.24	3.02	2.36	2.61	18.20	<0.001	0.12
Generalised Anxiety	7.31	3.78	7.62	3.72	5.25	3.53	12.30	<0.001	0.09
Total	39.29	18.70	40.11	17.61	25.71	16.95	20.56	<0.001	0.13

2.6.1 Sleep as a predictor of Panic Symptoms

Sleep disturbances were significantly associated with Panic Symptoms in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Panic Symptoms and CSHQ variables are presented in Table 2.6. In the Autism group, composite sleep scores were significant predictors of panic symptoms (ΔR^2 = 0.30, $\Delta F_{(8,45)}$ =2.69, p = 0.02), as well as the subscales of Sleep Onset Delay (**ß**=0.30, p=0.05), Sleep Anxiety (**ß**=0.37, p=0.05), and Daytime Sleepiness (**ß**=0.37, p=0.01). In the FASD group, composite sleep scores were significant predictors of Panic Symptoms (ΔR^2 = 0.26, $\Delta F_{(8,95)}$ =4.38, p = <0.001), as well as the subscale of Sleep Duration (**ß**=0.33, p=0.03). In the TD group, composite sleep scores were significant predictors of Panic Symptoms (ΔR^2 = 0.33, $\Delta F_{(8,91)}$ =5.86, p = <0.001), as well as the subscales of Sleep Onset Delay (**ß**=0.25, p=0.02), Sleep Anxiety (**ß**=0.27, p=0.05), Parasomnia (**ß**=0.24, p=0.015), and Daytime Sleepiness (**ß**=0.277, p=0.011). Sleep disturbances explained 38% of the variance in Panic Symptoms in the Autism group, 30% in the FASD group and 35% in the TD group after controlling for age, SES and sex.

Group comparisons in the subscale of Panic

Raw Score: Overall, the tests of between subject effects on the SCAS subscale of Panic Symptoms showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=30.24, p=<0.001, R^2=0.19). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher), and significant similarity between the Autism/ FASD groups when using the range of acceptability of 10% (p=0.05; both scoring very similarly). *Age*: There were significant age associations in in the Autism ($F_{(1, 58)}$=4.89, p=0.03, R^2=0.08), FASD ($F_{(1, 105)}$=4.76, p=0.03, R^2=0.04) and TD groups ($F_{(1, 102)}$=1.20, p=0.01, R^2=0.27), with older children scoring higher than younger children. Sex and SES were not significant predictors of Panic in any of the groups.

Table 2.6: Hierarchical multiple regression results for SCAS Subscale Panic Symptoms

			Overall Model			**Change Statistics**		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	0.79	3.32		0.08	4.80	0.08
n= 68		Age	0.05	0.02	**0.29***			
		Sex	0.81	1.64	0.07			
		SES	-0.55	1.06	-0.07			
	2	(Constant)	15.41	4.76		0.30	2.69	**0.38***
		Age	0.03	0.02	0.15			
		Sex	1.43	1.59	0.12			
		SES	1.27	1.10	0.16			
		Bedtime Resistance	0.43	0.30	0.28			
		Sleep Onset Delay	***2.02***	***0.98***	***0.30****			
		Sleep Duration	0.54	0.46	0.17			
		Sleep Anxiety	***0.67***	***0.33***	***0.37****			
		Night Wakings	-0.17	0.48	-0.06			
		Parasomnia	0.08	0.20	0.05			
		Sleep Disordered Breathing	0.19	0.37	0.07			
		Daytime Sleepiness	***0.52***	***0.19***	***0.37****			
FASD	1	(Constant)	2.58	2.20		0.04	4.76	0.04
n=105		Age	0.03	0.01	0.20			
		Sex	-0.24	0.88	-0.03			
		SES	0.24	0.74	0.03			
	2	(Constant)	10.58	3.55		0.26	4.38	**0.30****
		Age	0.03	0.01	0.23			
		Sex	0.00	0.80	0.00			
		SES	0.61	0.70	0.08			
		Bedtime Resistance	0.01	0.20	0.01			
		Sleep Onset Delay	0.10	0.68	0.02			
		Sleep Duration	***0.77***	***0.25***	***0.33****			
		Sleep Anxiety	0.34	0.21	0.22			
		Night Wakings	0.21	0.27	0.09			
		Parasomnia	0.12	0.14	0.10			
		Sleep Disordered Breathing	0.42	0.24	0.18			
		Daytime Sleepiness	0.21	0.14	0.14			
TD	1	(Constant)	0.84	1.64		0.01	1.20	0.01
n=101		Age	0.01	0.01	0.12			
		Sex	0.43	0.58	0.08			
		SES	0.04	0.50	0.01			
	2	(Constant)	7.39	2.07		0.33	5.86	**0.35****
		Age	0.00	0.01	0.04			
		Sex	0.09	0.51	0.02			
		SES	0.79	0.46	0.16			
		Bedtime Resistance	0.11	0.12	0.11			
		Sleep Onset Delay	***0.92***	***0.40***	***0.25****			
		Sleep Duration	0.28	0.19	0.15			
		Sleep Anxiety	***0.33***	***0.17***	***0.27****			
		Night Wakings	0.15	0.22	0.06			
		Parasomnia	***0.23***	***0.09***	***0.24****			
		Sleep Disordered Breathing	0.35	0.20	0.17			
		Daytime Sleepiness	***0.22***	***0.09***	***0.28****			

***p*=<0.05, ** *p*=<0.001.**

2.6.2 Sleep as a predictor of Separation Anxiety

Sleep disturbances were significantly associated with Separation Anxiety in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Separation Anxiety and CSHQ variables are presented in Table 2.7. In the Autism group, composite sleep scores were significant predictors of Separation Anxiety (ΔR^2=0.46, $\Delta F_{(8,61)}$=4.98, p=<0.001), as well as the subscale of Parasomnia (**ß**=0.32, p=0.02). In the FASD group, composite sleep scores were significant predictors of Separation Anxiety (ΔR^2 = 0.35, $\Delta F_{(8,95)}$ =4.38, p=<0.001), as well as the subscale of Sleep Anxiety (**ß**=0.39, p=<0.001). In the TD group, composite sleep scores were significant predictors of Separation Anxiety (ΔR^2=0.33, $\Delta F_{(8,91)}$ =5.86, p=<0.001), as well as the subscales of Bedtime Resistance (**ß**=0.31, p=0.01) and SDB (**ß**=0.21, p=0.03). Sleep disturbances explained 48% of the variance in Separation Anxiety in the Autism group, 43% in the FASD group and 42% in the TD group after controlling for age, SES and sex.

Group comparisons in the subscale of Separation Anxiety.

Raw Score: Overall, the tests of between subject effects on the SCAS subscale of Separation Anxiety showed significant differences between the three groups, with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=11.56, p=<0.001, R^2=0.08). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher), and significant similarity between the Autism/ FASD groups when using the range of acceptability of 10% (p=<0.05; both scoring very similarly). *Sex*: There were no significant overall Sex differences in the Autism or TD groups but in the FASD group, girls scored significantly higher than boys (Fem: m=8.45 SD=4.19; Male: m=7.96, SD=5.19 conditions t(105.0)=0.54, p=0.02). *Age*: Age was a significant predictor in the FASD ($F_{(1, 105)}$=51.15, p=0.03, R^2=0.04) and TD groups ($F_{(1, 102)}$=5.27, p=0.02, R^2=0.05), with older children scoring higher than younger children. SES was not a significant predictor of Separation Anxiety in any of the groups.

Table 2.7: Hierarchical multiple regression results for SCAS subscale Separation Anxiety

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	11.24	2.90		0.02	1.02	0.02
n= 68		Age	0.02	0.02	0.13			
		Sex	0.56	1.43	0.05			
		SES	0.53	0.93	0.08			
	2	(Constant)	0.01	3.68		0.46	4.98	**0.48****
		Age	0.01	0.02	0.07			
		Sex	0.72	1.23	0.07			
		SES	0.19	0.85	0.03			
		Bedtime Resistance	0.01	0.23	0.01			
		Sleep Onset Delay	0.08	0.76	0.01			
		Sleep Duration	0.19	0.35	0.07			
		Sleep Anxiety	0.84	0.25	0.55			
		Night Wakings	0.27	0.37	0.12			
		Parasomnia	***0.38***	***0.16***	***0.32****			
		Sleep Disordered Breathing	0.38	0.28	0.18			
		Daytime Sleepiness	0.18	0.14	0.15			
FASD	1	(Constant)	14.69	2.23		0.04	4.76	0.04
n=105		Age	-0.03	0.01	-0.22			
		Sex	0.79	0.89	0.08			
		SES	1.34	0.75	0.17			
	2	(Constant)	0.31	3.33		0.35	4.38	**0.43****
		Age	-0.02	0.01	-0.13			
		Sex	0.51	0.75	0.06			
		SES	0.52	0.65	0.07			
		Bedtime Resistance	0.07	0.19	0.05			
		Sleep Onset Delay	0.19	0.64	0.03			
		Sleep Duration	0.29	0.23	0.12			
		Sleep Anxiety	***0.61***	***0.20***	***0.39*****			
		Night Wakings	0.35	0.25	0.14			
		Parasomnia	0.12	0.13	0.10			
		Sleep Disordered Breathing	0.04	0.23	0.01			
		Daytime Sleepiness	0.03	0.14	0.02			
TD	1	(Constant)	7.25	2.59		0.01	1.20	0.05
n=101		Age	-0.03	0.02	-0.21			
		Sex	0.68	0.91	0.07			
		SES	0.70	0.78	0.09			
	2	(Constant)	8.09	3.16		0.33	5.86	**0.42****
		Age	-0.02	0.01	-0.16			
		Sex	0.86	0.77	0.09			
		SES	1.51	0.70	0.19			
		Bedtime Resistance	***0.48***	***0.19***	***0.31****			
		Sleep Onset Delay	0.27	0.61	0.05			
		Sleep Duration	0.11	0.29	0.04			
		Sleep Anxiety	0.34	0.25	0.17			
		Night Wakings	0.10	0.33	0.03			
		Parasomnia	0.22	0.14	0.14			
		Sleep Disordered Breathing	***0.68***	***0.30***	***0.21****			
		Daytime Sleepiness	0.04	0.13	0.03			

***p=<0.05, **p=<0.001.**

2.6.3 Sleep as a predictor of Physical Injury

Sleep disturbances significantly associated with Physical Injury symptoms in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Physical Injury symptoms and CSHQ variables are presented in Table 2.8. In the Autism group, composite sleep scores were significant predictors of Physical Injury symptoms (ΔR^2=0.45, $\Delta F_{(1,55)}$ =4.99, p=<0.001), as well as in the subscale of Sleep Anxiety (**ß**=0.74, p=<0.001). In the FASD group, composite sleep scores were significant predictors of Physical Injury symptoms (ΔR^2=0.20, $\Delta F_{(1,105)}$ =2.96, p=<0.001), as well as the subscale of Sleep Anxiety(**ß**=0.38, p=0.01). In the TD group, composite sleep scores were significant predictors of Physical Injury symptoms (ΔR^2=0.42, $\Delta F_{(1,101)}$ =8.58, p=<0.001), as well as the subscales of Sleep Onset Delay (**ß**=0.27, p=0.01), Sleep Anxiety (**ß**=0.41, p=<0.001) and SDB (**ß**=0.19, p=0.03). Sleep disturbances explained 48% of the variance in Physical Injury symptoms in the Autism group, 49% in the FASD group and 44% in the TD group after controlling for age, SES and sex.

Group comparisons in the subscale of Physical Injury symptoms

Raw Score: Overall, the tests of between subject effects on the SCAS subscale of Physical Injury symptoms showed no significant differences between the three groups ($F_{(2, 266)}$=2.92, p=0.06, R^2=0.02). In post-hoc analysis and tests of similarity, there were no significant differences in raw scores between the TD/ Autism and TD/FASD groups, but there was significant similarity between the Autism/ FASD groups when using the range of acceptability of 10% (p=<0.05; both scoring very similarly). *Sex*: There were no significant overall differences in the FASD or TD groups, however in the Autism group, boys scored significantly higher than girls (Fem: m=5.51 SD=3.17; Male: m=5.12, SD=3.17 conditions t(56.0)=-0.17, p=0.01). Sex and age were not significant predictors of Physical Injury Symptoms in any of the groups.

Table 2.8: Hierarchical multiple regression results for SCAS subscale Physical Injury

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	8.20	2.17		0.03	1.80	0.02
n= 68		Age	-0.02	0.02	-0.18			
		Sex	0.24	1.07	0.03			
		SES	-0.22	0.70	-0.04			
	2	(Constant)	1.45	2.76		0.45	4.99	**0.48****
		Age	-0.02	0.01	-0.21			
		Sex	-0.18	0.92	-0.02			
		SES	0.58	0.64	0.11			
		Bedtime Resistance	0.07	0.17	0.07			
		Sleep Onset Delay	0.38	0.57	0.09			
		Sleep Duration	0.12	0.26	0.06			
		Sleep Anxiety	***0.86***	***0.19***	***0.74*****			
		Night Wakings	0.41	0.28	0.23			
		Parasomnia	0.06	0.12	0.07			
		Sleep Disordered Breathing	0.37	0.21	0.23			
		Daytime Sleepiness	0.21	0.11	0.23			
FASD	1	(Constant)	5.70	1.57		0.01	0.64	0.03
n=105		Age	0.01	0.01	0.06			
		Sex	-0.75	0.63	-0.12			
		SES	-0.24	0.53	-0.05			
	2	(Constant)	0.67	2.66		0.20	2.96	**0.49****
		Age	0.01	0.01	0.13			
		Sex	-0.60	0.60	-0.10			
		SES	0.26	0.52	0.05			
		Bedtime Resistance	0.01	0.15	0.02			
		Sleep Onset Delay	0.22	0.51	0.05			
		Sleep Duration	0.08	0.19	0.05			
		Sleep Anxiety	***0.41***	***0.16***	***0.38****			
		Night Wakings	0.16	0.20	-0.09			
		Parasomnia	0.16	0.10	0.19			
		Sleep Disordered Breathing	0.13	0.18	0.08			
		Daytime Sleepiness	0.01	0.11	0.01			
TD	1	(Constant)	5.19	1.87		0.00	0.35	0.01
n=101		Age	-0.01	0.01	-0.08			
		Sex	0.75	0.66	0.12			
		SES	-0.03	0.57	-0.01			
	2	(Constant)	4.06	2.19		0.42	8.58	**0.44****
		Age	-0.00	0.01	-0.01			
		Sex	0.96	0.54	0.15			
		SES	-0.60	0.49	-0.11			
		Bedtime Resistance	0.07	0.13	0.06			
		Sleep Onset Delay	***1.13***	***0.42***	***0.27****			
		Sleep Duration	0.18	0.20	0.09			
		Sleep Anxiety	***0.58***	***0.17***	***0.41****			
		Night Wakings	0.26	0.23	0.10			
		Parasomnia	0.35	0.10	0.32			
		Sleep Disordered Breathing	***0.45***	***0.21***	***0.19****			
		Daytime Sleepiness	0.03	0.09	0.03			

***p=<0.05, ** p=<0.001**

2.6.4 Sleep as a predictor of Social Phobia

Sleep disturbances were significantly associated with Social Phobia symptoms in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Social Phobia and CSHQ variables are presented in Table 2.9. In the Autism group, composite sleep scores were significant predictors of Social Phobia (ΔR^2=0.46, $\Delta F_{(8,55)}$ =4.98, p =<0.001), but individual CHSQ subscales were not. In the FASD group, composite sleep scores were significant predictors of Social Phobia (ΔR^2 = 0.35, $\Delta F_{(8,95)}$ =4.38, p =<0.001), as well as the subscale of Daytime Sleepiness (**ß**=0.24, p=0.02). In the TD group, composite sleep scores were significant predictors of Social Phobia (ΔR^2=0.33, $\Delta F_{(8,91)}$ =5.86, p = <0.001), as well as the subscale of SDB (**ß**=0.14, p=0.03). Sleep disturbances explained 48% of the variance in Social Phobia symptoms in the Autism group, 43% in the FASD group and 42% in the TD group after controlling for age, SES and sex.

Group comparisons in the subscale of Social Phobia

Raw Score: Overall, the tests of between subject effects on the SCAS subscale of Social Phobia showed significant differences between the three groups, with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=7.975, p=<0.001, R^2=0.06). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher). *Age*: There were significant age related associations in the TD ($F_{(1, 102)}$=4.42, p=0.04, R^2=0.27), and FASD groups ($F_{(1, 105)}$=13.31, p=<0.001, R^2=0.11) with older children scoring higher, but not in the Autism group. SES and sex were not significant predictors of Social Phobia in any of the groups.

Table 2.9: Hierarchical multiple regression results for SCAS subscale Social Phobia

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	8.38	2.80		0.02	1.02	0.02
n= 68		Age	0.02	0.02	0.13			
		Sex	0.01	1.39	0.00			
		SES	-1.54	0.90	-0.23			
	2	(Constant)	1.36	4.52		0.46	4.98	**0.48****
		Age	0.01	0.02	0.05			
		Sex	0.36	1.51	0.03			
		SES	-0.42	1.04	-0.06			
		Bedtime Resistance	0.32	0.28	0.25			
		Sleep Onset Delay	1.10	0.94	0.20			
		Sleep Duration	0.11	0.43	0.04			
		Sleep Anxiety	0.59	0.31	0.39			
		Night Wakings	0.42	0.45	0.18			
		Parasomnia	0.11	0.19	0.09			
		Sleep Disordered Breathing	0.08	0.35	0.04			
		Daytime Sleepiness	0.18	0.18	0.16			
FASD	1	(Constant)	4.01	2.12		0.04	4.76	0.04
n=105		Age	0.04	0.01	0.31			
		Sex	-1.61	0.85	-0.18			
		SES	0.24	0.71	0.03			
	2	(Constant)	7.21	3.63		0.35	4.38	**0.43****
		Age	0.05	0.01	0.37			
		Sex	-1.38	0.82	-0.15			
		SES	0.52	0.71	0.07			
		Bedtime Resistance	0.21	0.21	0.15			
		Sleep Onset Delay	0.51	0.70	0.08			
		Sleep Duration	0.30	0.26	0.13			
		Sleep Anxiety	0.20	0.22	0.13			
		Night Wakings	0.18	0.28	0.07			
		Parasomnia	-0.20	0.14	-0.17			
		Sleep Disordered Breathing	0.02	0.25	0.01			
		Daytime Sleepiness	***0.34***	***0.15***	***0.24****			
TD	1	(Constant)	1.96	2.49		0.01	1.20	0.05
n=101		Age	0.03	0.01	0.21			
		Sex	0.01	0.88	0.00			
		SES	0.42	0.76	0.06			
	2	(Constant)	6.61	3.53		0.33	5.86	**0.42****
		Age	0.02	0.02	0.16			
		Sex	0.52	0.87	0.06			
		SES	1.15	0.78	0.16			
		Bedtime Resistance	0.00	0.21	0.00			
		Sleep Onset Delay	0.40	0.68	0.07			
		Sleep Duration	0.05	0.32	0.02			
		Sleep Anxiety	0.13	0.28	0.07			
		Night Wakings	0.10	0.37	0.03			
		Parasomnia	0.41	0.16	0.28			
		Sleep Disordered Breathing	***0.45***	***0.34***	***0.14****			
		Daytime Sleepiness	0.23	0.15	0.19			

******p*=<0.05, ** *p*=<0.001.**

2.6.5 Sleep as a predictor of Obsessive-Compulsive symptoms

Sleep disturbances were significantly associated with Obsessive-Compulsive symptoms in the TD and FASD groups, but not the Autism group. Hierarchical multiple regression results examining the associations between Obsessive-Compulsive symptoms and CSHQ variables are presented in Table 2.10. In the Autism group, composite sleep scores were not significant predictors of Obsessive-Compulsive symptoms ($\Delta R^2 = 0.17$, $\Delta F_{(8,45)} = 1.18$, $p = 0.34$) and neither were any of the CSHQ subscales. In the FASD group, composite sleep scores were not significant predictors of Obsessive-Compulsive symptoms ($\Delta R^2 = 0.13$, $\Delta F_{(8,95)} = 1.82$, $p = 0.08$), but the subscale of Sleep Duration (**ß**=0.26, $p = 0.03$) was. In the TD group however, composite sleep scores were significant predictors of Obsessive-Compulsive symptoms ($\Delta R^2 = 0.29$, $\Delta F_{(8,91)} = 4.80$, $p = 0.01$), as well as the subscales of SDB (**ß** = 0.31, $p = 0.01$) and Daytime Sleepiness (**ß**= 0.27, $p = 0.04$). Sleep disturbances did not (significantly) explain the variance in the Autism or FASD groups but did explain 35% of the variance in the TD group after controlling for age, SES and sex.

Group comparisons in the subscale of Obsessive-Compulsive symptoms

Raw Score: Overall, the tests of between subject effects on the SCAS subscale of Obsessive-Compulsive symptoms showed significant differences between the three groups, with clinical groups scoring higher than the TD group ($F_{(2, 266)} = 18.20$, $p = <0.001$, $R^2 = 0.12$). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism ($p = <0.001$; Autism group scoring higher) and TD/FASD groups ($p = <0.001$; FASD group scoring higher), and significant similarity between the Autism/ FASD groups when using the range of acceptability of 10% ($p = 0.05$; both scoring very similarly). Age, sex and SES were not significant predictors of Obsessive-Compulsive symptoms in any of the groups.

Table 2.10: Hierarchical multiple regression results for SCAS subscale Obsessive-Compulsive

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	5.27	2.50		0.00	0.17	0.00
n= 68		Age	0.01	0.02	0.06			
		Sex	-0.51	1.24	-0.06			
		SES	0.49	0.80	0.08			
	2	(Constant)	1.59	3.96		0.17	1.18	0.19
		Age	0.01	0.02	0.05			
		Sex	-0.41	1.32	-0.05			
		SES	0.27	0.91	0.05			
		Bedtime Resistance	0.24	0.25	0.22			
		Sleep Onset Delay	0.24	0.82	0.05			
		Sleep Duration	0.10	0.38	0.04			
		Sleep Anxiety	0.45	0.27	0.34			
		Night Wakings	0.38	0.40	0.19			
		Parasomnia	0.05	0.17	0.05			
		Sleep Disordered Breathing	0.10	0.30	0.05			
		Daytime Sleepiness	0.20	0.16	0.20			
FASD	1	(Constant)	2.42	1.48		0.00	0.14	<0.01
n=105		Age	0.00	0.01	0.03			
		Sex	0.44	0.59	0.07			
		SES	0.93	0.50	0.18			
	2	(Constant)	-3.59	2.60		0.13	1.82	0.17
		Age	0.00	0.01	0.02			
		Sex	0.31	0.59	0.05			
		SES	1.12	0.51	0.22			
		Bedtime Resistance	0.12	0.15	0.14			
		Sleep Onset Delay	0.09	0.50	0.02			
		Sleep Duration	***0.40***	***0.18***	***0.26****			
		Sleep Anxiety	0.17	0.16	0.17			
		Night Wakings	0.03	0.20	0.02			
		Parasomnia	0.08	0.10	0.11			
		Sleep Disordered Breathing	0.19	0.18	0.12			
		Daytime Sleepiness	0.10	0.11	0.10			
TD	1	(Constant)	1.51	1.49		0.02	1.93	0.02
n=101		Age	0.01	0.01	0.14			
		Sex	-0.41	0.53	-0.08			
		SES	-0.15	0.45	-0.04			
	2	(Constant)	-5.41	1.93		0.29	4.80	**0.32***
		Age	0.01	0.01	0.09			
		Sex	-0.10	0.47	-0.02			
		SES	0.52	0.43	0.12			
		Bedtime Resistance	0.00	0.12	0.00			
		Sleep Onset Delay	0.28	0.37	0.09			
		Sleep Duration	0.18	0.18	0.11			
		Sleep Anxiety	0.23	0.15	0.21			
		Night Wakings	0.04	0.20	0.02			
		Parasomnia	0.12	0.09	0.14			
		Sleep Disordered Breathing	***0.58***	***0.19***	***0.31****			
		Daytime Sleepiness	***0.20***	***0.08***	***0.27****			

***p*=<0.05, ** *p*=<0.001.**

2.6.6 Sleep as a predictor of Generalised Anxiety

Sleep disturbances were associated with Generalised Anxiety in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Generalised Anxiety and CSHQ variables are presented in Table 2.11. In the Autism group, composite sleep scores were not significant predictors of Generalised Anxiety (ΔR^2 = 0.21, $\Delta F_{(8,45)}$ =1.68, p=0.13), as well as the subscale of Sleep Anxiety (**ß**=0.52, p=<0.001). In the FASD group, composite sleep scores were not significant predictors of Generalised Anxiety (ΔR^2 =0.11, $\Delta F_{(8,95)}$ =1.45, p=0.19). In the TD group, composite sleep scores were significant predictors of Generalised Anxiety (ΔR^2=0.31, $\Delta F_{(8,91)}$=5.18, p=0.01), as well as the subscales of Sleep Disordered Breathing (**ß**=0.29,p=0.02) and Daytime Sleepiness (**ß**=0.29, p=0.01). Sleep disturbances explained 29% of the variance in Generalised Anxiety in the Autism group, 12% in the FASD group (nonsignificant results) and 32% in the TD group after controlling for age, SES and sex.

Group comparisons in the subscale of Generalised Anxiety

Raw Score: Overall, the tests of between subject effects on the SCAS subscale of Generalised Anxiety showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=12.30, p=<0.001, R^2=0.09). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism groups scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher), and significant similarity between the Autism/ FASD groups when using the range of acceptability of 10% (p=0.05; both scoring very similarly). Age, sex and SES were not significant predictors of Generalised Anxiety in any of the groups.

Table 2.11: Hierarchical multiple regression results for SCAS subscale Generalised Anxiety

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	4.08	2.42		0.06	3.73	0.06
n= 68		Age	0.03	0.02	0.26			
		Sex	0.81	1.20	0.09			
		SES	0.39	0.78	0.07			
	2	(Constant)	3.00	3.71		0.21	1.68	0.29
		Age	0.03	0.02	0.26			
		Sex	1.36	1.24	0.15			
		SES	0.12	0.86	0.02			
		Bedtime Resistance	0.45	0.23	0.40			
		Sleep Onset Delay	0.43	0.77	0.09			
		Sleep Duration	0.08	0.36	0.03			
		Sleep Anxiety	***0.68***	***0.26***	***0.52****			
		Night Wakings	0.10	0.37	0.05			
		Parasomnia	0.21	0.16	0.21			
		Sleep Disordered Breathing	-0.07	0.29	-0.04			
		Daytime Sleepiness	0.08	0.15	0.08			
FASD	1	(Constant)	6.14	1.85		0.01	0.92	0.01
n=105		Age	0.01	0.01	0.10			
		Sex	0.26	0.74	0.04			
		SES	0.04	0.62	0.01	0.11	1.45	0.12
	2	(Constant)	1.55	3.30				
		Age	0.01	0.01	0.11			
		Sex	0.43	0.75	0.06			
		SES	0.21	0.65	0.03			
		Bedtime Resistance	-0.16	0.19	-0.15			
		Sleep Onset Delay	0.72	0.63	0.14			
		Sleep Duration	0.24	0.23	0.12			
		Sleep Anxiety	0.37	0.20	0.30			
		Night Wakings	0.17	0.25	0.08			
		Parasomnia	0.01	0.13	0.01			
		Sleep Disordered Breathing	0.35	0.23	0.17			
		Daytime Sleepiness	0.05	0.13	0.04			
TD	1	(Constant)	4.30	2.02		0.01	0.93	0.01
n=101		Age	0.01	0.01	0.10			
		Sex	-0.48	0.71	-0.07			
		SES	-0.07	0.61	-0.01			
	2	(Constant)	-5.74	2.59		0.31	5.18	**0.32***
		Age	0.00	0.01	0.03			
		Sex	0.01	0.64	0.00			
		SES	0.77	0.58	0.13			
		Bedtime Resistance	0.03	0.16	0.03			
		Sleep Onset Delay	0.05	0.50	0.01			
		Sleep Duration	0.29	0.24	0.13			
		Sleep Anxiety	0.36	0.21	0.23			
		Night Wakings	0.11	0.27	0.04			
		Parasomnia	0.20	0.12	0.16			
		Sleep Disordered Breathing	***0.74***	***0.25***	***0.29****			
		Daytime Sleepiness	***0.28***	***0.11***	***0.29****			

***p*=<0.05, ** *p*=<0.001.**

2.6.7 Sleep as a predictor of Anxiety (composite)

Sleep disturbances were significantly associated with SCAS Total scores in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between SCAS Total and CSHQ variables are presented in Table 2.12. In the Autism group, composite sleep scores were significant predictors of SCAS Total score (ΔR^2=0.37, $\Delta F_{(8,45)}$ =3.38, p = <0.001), as well as the subscale of Sleep Anxiety (**ß**=0.62, p= <0.001). In the FASD group, composite sleep scores were significant predictors of SCAS Total score (ΔR^2 = 0.29, $\Delta F_{(8,95)}$ =5.03, p = <0.001), as well as the subscales of Sleep Duration (**ß**=0.23, p=0.03) and Sleep Anxiety (**ß**=0.23, p=0.03). In the TD group, composite sleep scores were significant predictors of SCAS Total score (ΔR^2 = 0.40, $\Delta F_{(8,91)}$ =7.53, p = <0.001), as well as the subscales of Sleep Anxiety (**ß**=0.27, p=0.04), Parasomnia (**ß**=0.27, p=0.01), and SDB (**ß**=0.27, p=0.01). Sleep disturbances explained 39% of the variance in SCAS Total scores in the Autism group, 32% in the FASD group and 40% in the TD group after controlling for age, SES and sex.

Group comparisons in Anxiety Composite Score

Raw Score: Overall, the tests of between subject effects on the SCAS Total showed significant differences between the three groups, with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=20.56, p=<0.001, R^2=0.13). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher), and significant similarity between the Autism/ FASD groups when using the range of acceptability of 10% (p=0.05; both scoring very similarly). *Sex*: There were significant overall sex differences in the FASD and TD groups, with girls scoring significantly higher than boys, however none in the Autism group (FASD: Fem: m=42.51 SD=3.17; Male: m=37.12, SD=3.17 conditions t(56.0)=-0.17, p=0.01; TD Fem: m=26.51 SD=9.17; Male: m=23.12, SD=6.17 conditions t(56.0)=-0.17, p=0.01). SES and Age were not significant predictors of SCAS composite scores.

Table 2.12: Hierarchical multiple regression results for SCAS Total

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	37.95	12.32		0.01	0.60	0.01
n= 68		Age	0.07	0.08	0.11			
		Sex	0.79	6.09	0.02			
		SES	-3.71	3.95	-0.13			
	2	(Constant)	20.05	16.97		0.37	3.38	**0.39****
		Age	0.04	0.08	0.06			
		Sex	1.81	5.67	0.04			
		SES	-1.08	3.92	-0.04			
		Bedtime Resistance	1.52	1.07	0.27			
		Sleep Onset Delay	4.04	3.51	0.17			
		Sleep Duration	0.95	1.62	0.09			
		Sleep Anxiety	***4.09***	***1.17***	***0.62****			
		Night Wakings	0.79	1.70	0.08			
		Parasomnia	0.77	0.72	0.15			
		Sleep Disordered Breathing	1.06	1.31	0.12			
		Daytime Sleepiness	1.01	0.67	0.20			
FASD	1	(Constant)	34.53	8.66		0.01	1.52	0.01
n=105		Age	0.05	0.05	0.10			
		Sex	-4.38	3.46	-0.12			
		SES	0.75	2.91	0.03			
	2	(Constant)	-18.77	13.72		0.29	5.03	**0.32****
		Age	0.08	0.05	0.16			
		Sex	-3.32	3.10	-0.09			
		SES	2.91	2.70	0.10			
		Bedtime Resistance	0.15	0.79	0.03			
		Sleep Onset Delay	1.18	2.63	0.05			
		Sleep Duration	***2.10***	***0.97***	***0.23****			
		Sleep Anxiety	***1.86***	***0.82***	***0.31****			
		Night Wakings	0.06	1.04	0.01			
		Parasomnia	0.37	0.54	0.08			
		Sleep Disordered Breathing	1.17	0.94	0.12			
		Daytime Sleepiness	0.35	0.56	0.06			
TD	1	(Constant)	21.06	9.76		0.00	0.16	<0.01
n=101		Age	0.03	0.06	0.05			
		Sex	0.03	3.44	0.00			
		SES	0.90	2.96	0.03			
	2	(Constant)	37.72	11.72		0.40	7.53	**0.40****
		Age	0.01	0.05	0.02			
		Sex	2.27	2.87	0.07			
		SES	5.36	2.60	0.19			
		Bedtime Resistance	0.29	0.70	0.05			
		Sleep Onset Delay	2.39	2.25	0.11			
		Sleep Duration	0.32	1.06	0.03			
		Sleep Anxiety	***1.97***	***0.93***	***0.27****			
		Night Wakings	0.58	1.22	0.04			
		Parasomnia	***1.53***	***0.53***	***0.27****			
		Sleep Disordered Breathing	***3.24***	***1.12***	***0.27****			
		Daytime Sleepiness	1.01	0.48	0.22			

***p*=<0.05, ** *p*=<0.001.**

2.6.8 Summary

Apart from Physical Injury Fears, children with FASD and Autism scored consistently higher than TD children in SCAS total and subscales. The two clinical groups scored higher than the TD group in the subscales of Panic, Separation Anxiety, Obsessive Compulsive, Generalised Anxiety and Total Score. In the subscale of Social Phobia, the FASD group scored higher than the TD group, but the TD and Autism groups did not significantly differ. The two clinical groups scored significantly similarly in the SCAS subscales of Panic, Separation Anxiety, Physical Injury, Generalised Anxiety, and SCAS Total (See Figure 2.2).

Age was a significant predictor of Panic Symptoms in the Autism, FASD and TD groups; Separation Anxiety in the FASD and TD groups, and Social Phobia in the TD group, with older children tending to score higher. Girls scored significantly higher than boys in the FASD group for in Separation Anxiety whilst boys scored significantly higher than girls in the Autism group for Physical Injury. Girls scored significantly higher in the FASD and TD groups for SCAS total, but not in the Autism group.

Sleep disturbance was significantly associated with anxiety in all three groups, with more sleep problems significantly correlating with more anxiety problems. In the Autism group, Sleep Anxiety and Total CSHQ scores accounted for the largest amount of variance in anxiety symptoms; in total, 39% of the variance in anxiety scores was attributable to sleep problems. In the FASD group, Sleep Duration, Sleep Anxiety and CSHQ Total scores accounted for the largest amount of variance in anxiety symptoms; in total, 32% of the variance in anxiety scores was attributable to sleep problems. In the TD group, Sleep Onset Delay, SDB, Daytime Sleepiness and Total CSHQ scores accounted for the largest amount of variance in anxiety symptoms; in total, 40% of the variance in anxiety scores was attributable to sleep problems.

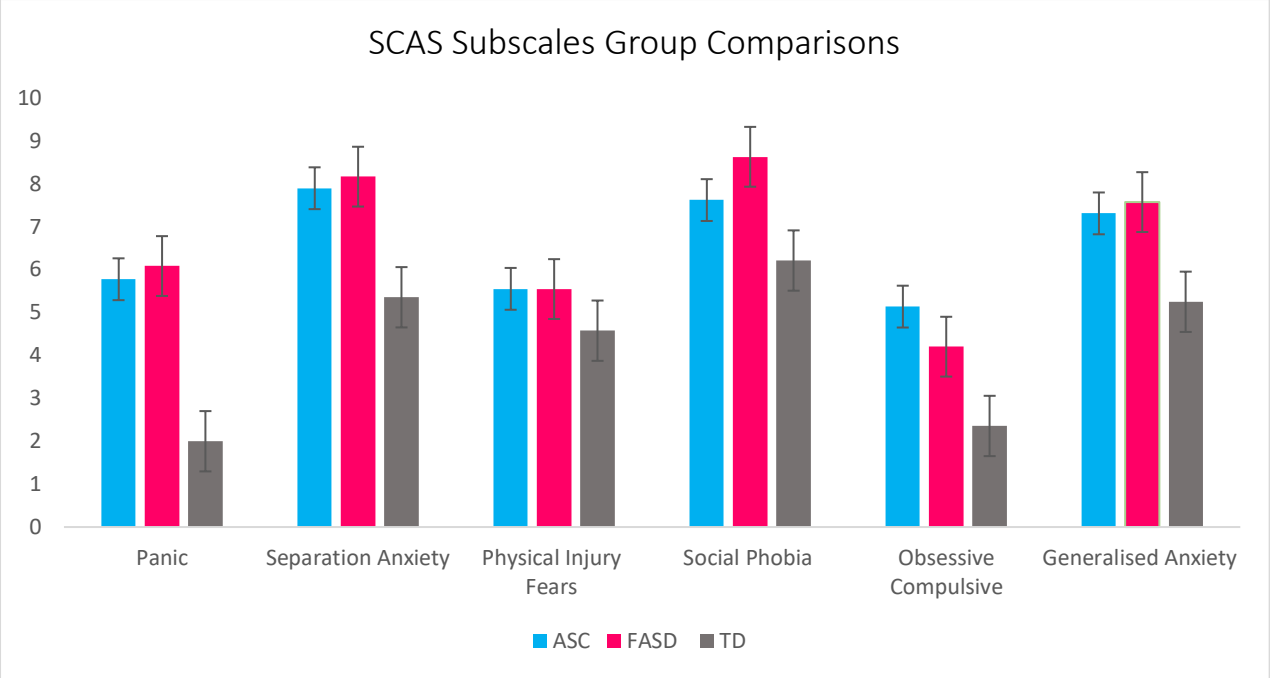


Figure 2.3: Comparison between Autism, FASD and TD scores on the SCAS Subscales (SE bars)

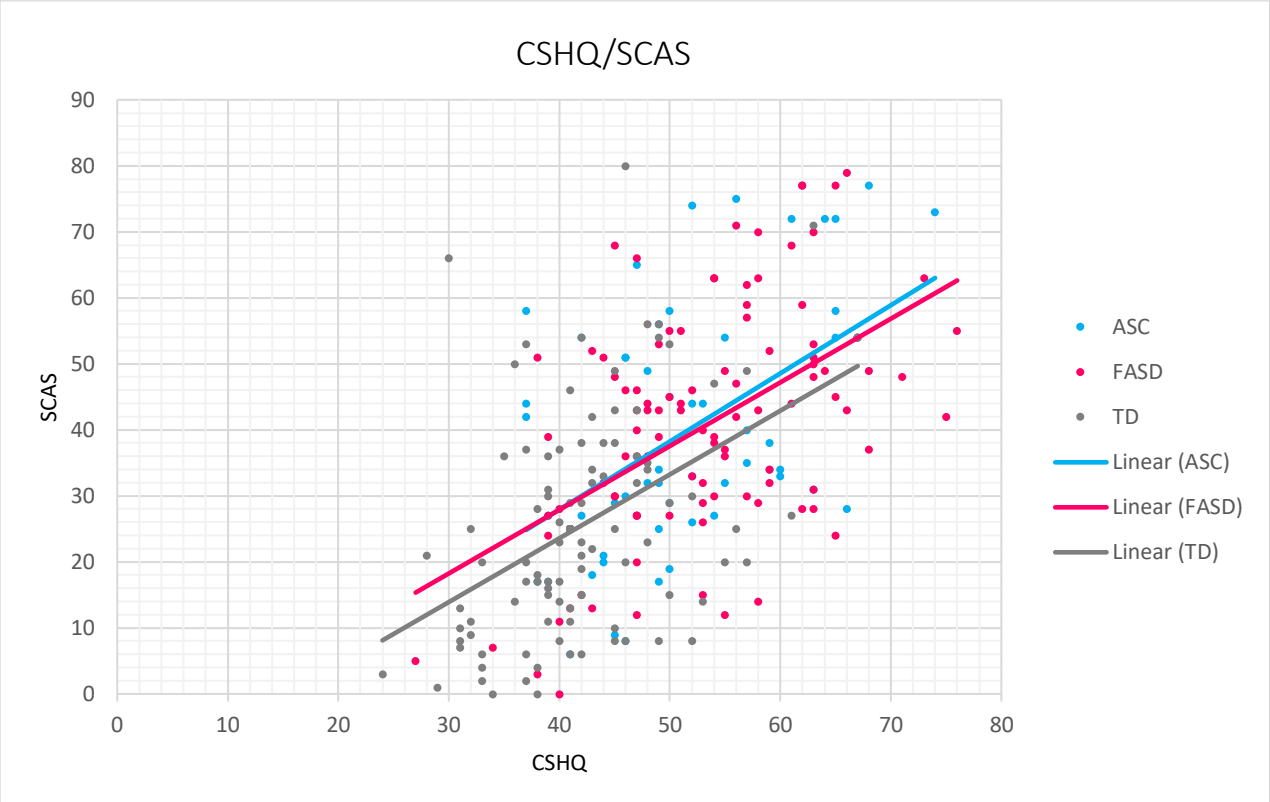


Figure 2.4: Scatter plot showing raw scores: sleep (CSHQ) against anxiety (SCAS)

2.7 Results: The Behavior Rating Inventory for Executive Functioning (BRIEF)

Executive Functioning is an overarching concept that underpins higher order processes, and it is the absence or reduction of these processes that contribute to (at least some of) the current definition of both FASD and Autism. Earlier, it was established that FASD and Autism differ in their unique executive function profiles. This is the first study to examine the executive function profiles of these two clinical groups together. The purpose of the following section is to find out whether, in the search for a unique FASD executive function profile, it may be necessary to differentiate it from other more well established executive function profiles, and to look at whether sleep can be seen as a substantial predictor of executive function components in both clinical groups.

The BRIEF variables were analysed using group mean comparisons. Effect sizes are displayed as partial eta squared (η_p^2). ANOVA results are presented in table 2.13. Hierarchical multiple regression analyses were conducted in order to examine the associations between each BRIEF subscale and CSHQ subscale. These are presented in tables 2.14 – 2.21.

Table 2.13: Mean Scores (SD) and group differences using ANOVA for BRIEF subsets

	Autism (n=61)		FASD (n=114)		TD (n=104)		F	p	ηp2
	m	sd	m	sd	m	sd			
Working Memory	27.41	15.82	24.97	4.38	15.50	5.33	48.20	<0.001	0.27
Shifting	23.64	18.61	19.46	3.73	12.32	4.48	30.49	<0.001	0.19
Planning and Organising	30.64	15.72	29.34	4.97	19.42	6.38	43.82	<0.001	0.25
Organisation of Materials	18.41	15.01	14.87	3.16	11.04	4.61	17.38	<0.001	0.12
Monitoring	23.43	17.08	19.92	3.30	13.55	4.63	27.37	<0.001	0.17
Inhibition	26.19	16.08	23.53	4.14	15.77	5.60	33.97	<0.001	0.20
Initiation	23.19	17.40	18.96	3.20	13.25	4.88	25.23	<0.001	0.16
Emotional Control	29.55	14.79	26.75	4.48	18.51	6.41	40.07	<0.001	0.23
Total	158.81	35.84	177.79	26.72	117.27	34.22	97.49	<0.001	0.42

2.7.1 Sleep as a predictor of Working Memory

Sleep disturbances were associated with Working Memory in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Working Memory and CSHQ variables are presented in Table 2.14. In the Autism group, composite sleep scores were significant predictors of Working Memory (ΔR^2 = 0.34, $\Delta F_{(1,55)}$ =3.35, p = 0.004), as well as the subscale of Sleep Onset Delay (**ß** = 0.32, p=0.03) and Sleep Duration (**ß** = 0.49, p=<0.001). In the FASD group, composite sleep scores were significant predictors of Working Memory (ΔR^2 = 0.22, $\Delta F_{(1,105)}$ =3.93, p = <0.001), as well as the subscales of Sleep Duration (**ß** = 0.24, p= 0.02) and Parasomnia (**ß** = 0.32, p= 0.01). In the TD group, composite sleep scores were significant predictors of Working Memory (ΔR^2 = 0.18, $\Delta F_{(1,101)}$ =2.716, p = 0.01), but not subscales. Sleep disturbances explained 42% of the variance in Working Memory scores in the Autism group, 33% in the FASD group and 25% in the TD group after controlling for age, SES and sex.

Group comparisons in Working Memory

Raw Score: Overall, the tests of between subject effects on the Working Memory subscale showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=48.20, p=<0.001, R^2=0.27). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher) but no significant similarities or differences in the Autism/FASD group. *SES*: There were significant SES differences in the FASD group ($F_{(2, 104)}$=3.46, p=0.04, R^2=0.07) with the lower SES group scoring higher than higher SES. *Sex*: There were significant differences between Autism boys and girls, with girls scoring higher than boys (Fem: m=29.24 SD=17.0; Male: m=21.08, SD=6.0 conditions t(1.66)=0.56, p=0.05). Age was not a predictor of Working Memory in any of the groups.

Table 2.14: Hierarchical multiple regression results for BRIEF Subscale Working Memory

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	42.3	10.09		0.01	0.47	0.01
n= 68		Age	0.04	0.07	0.08			
		Sex	7.48	4.99	0.20			
		SES	4.51	3.23	0.18			
	2	(Constant)	52.1	13.92		0.34	3.35	**0.42***
		Age	0.01	0.06	0.024			
		Sex	6.52	4.65	0.172			
		SES	7.22	3.21	0.295			
		Bedtime Resistance	1.42	0.87	0.30			
		Sleep Onset Delay	***6.55***	***2.88***	***0.32****			
		Sleep Duration	***4.59***	***1.33***	***0.49****			
		Sleep Anxiety	0.19	0.96	0.03			
		Night Wakings	0.31	1.40	0.04			
		Parasomnia	0.63	0.59	0.15			
		Sleep Disordered Breathing	-0.69	1.07	-0.09			
		Daytime Sleepiness	-1.15	0.55	-0.27			
FASD	1	(Constant)	25.90	2.07		0.04	4.23	0.04
n=105		Age	0.02	0.01	0.17			
		Sex	-1.26	0.83	-0.14			
		SES	-1.60	0.69	-0.22			
	2	(Constant)	16.66	3.39		0.22	3.93	**0.33****
		Age	0.02	0.01	0.17			
		Sex	-1.11	0.77	-0.13			
		SES	-1.25	0.67	-0.17			
		Bedtime Resistance	-0.10	0.19	-0.08			
		Sleep Onset Delay	0.72	0.65	0.12			
		Sleep Duration	***0.55***	***0.24***	***0.24****			
		Sleep Anxiety	0.26	0.20	0.17			
		Night Wakings	0.32	0.26	0.13			
		Parasomnia	***0.37***	***0.13***	***0.32****			
		Sleep Disordered Breathing	0.01	0.23	0.00			
		Daytime Sleepiness	0.01	0.14	0.01			
TD	1	(Constant)	13.52	2.97		0.03	2.62	0.03
n=101		Age	0.03	0.02	0.19			
		Sex	-2.37	1.05	-0.22			
		SES	-0.26	0.90	-0.03			
	2	(Constant)	4.94	4.13		0.18	2.72	**0.25***
		Age	0.01	0.02	0.06			
		Sex	-1.36	1.01	-0.13			
		SES	0.46	0.92	0.05			
		Bedtime Resistance	-0.37	0.25	-0.21			
		Sleep Onset Delay	0.04	0.79	0.01			
		Sleep Duration	0.66	0.37	0.20			
		Sleep Anxiety	0.57	0.33	0.25			
		Night Wakings	-0.11	0.43	-0.03			
		Parasomnia	0.18	0.19	0.10			
		Sleep Disordered Breathing	0.30	0.40	0.08			
		Daytime Sleepiness	0.33	0.17	0.22			

***p*=<0.05, ** *p*=<0.001.**

2.7.2 Sleep as a predictor of Shifting

Sleep disturbances were associated with Shifting in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Shifting and CSHQ variables are presented in Table 2.15. In the Autism group, composite sleep scores were significant predictors of Shifting (ΔR^2=0.41, $\Delta F_{(1,55)}$=4.54, p=<0.001), as well as the subscale of Sleep Onset Delay (**ß**=0.37, p=0.01), and Daytime Sleepiness (**ß** = 0.33, p=0.01). In the FASD group, composite sleep scores were significant predictors of Shifting (ΔR^2 = 0.35, $\Delta F_{(1,105)}$ =6.94, p = <0.001), as well as the subscale of Sleep Anxiety (**ß** = 0.38, p= 0.02) and Parasomnia (**ß** =0.40, p= 0.01). In the TD group, composite sleep scores were not significant predictors of Shifting (ΔR^2 = 0.15, $\Delta F_{(1,101)}$ =1.96, p = 0.10), or subscales. Sleep disturbances explained 42% of the variance in Shifting in the Autism group, 33% in the FASD group and 25% in the TD group after controlling for age, SES and sex.

Group comparisons in Shifting

Raw Score: Overall, the tests of between subject effects on the Shifting subscale showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=30.49, p=<0.001, R^2=0.19). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher), but no significant differences or similarities between the FASD and Autism groups. *SES*: There were significant SES differences in the Autism group ($F_{(2, 104)}$=4.87, p=0.01, R^2=0.09) with lower SES scoring higher than higher SES. *Sex*: There were significant differences between Autism and TD boys and girls, with girls scoring higher than boys in both groups (Autism: Fem: m=25.85 SD=20.00; Male: m=16.00, SD=4.89 conditions t(1.71)=56, p=0.02. TD: Fem: m=12.81=5.34; Male: m=11.69, SD=3.25 conditions t(1.26)=100, p=0.04). Age was not a significant predictor of Shifting in any of the groups.

Table 2.15: Hierarchical multiple regression results for BRIEF Subscale Shifting

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
ASC	1	(Constant)	42.94	11.87		0.02	1.35	0.02
n= 68		Age	-0.09	0.08	-0.14			
		Sex	-9.24	5.87	-0.21			
		SES	-3.61	3.81	-0.13			
	2	(Constant)	59.94	15.39		0.41	4.54	**0.50****
		Age	-0.01	0.07	-0.01			
		Sex	-8.32	5.14	-0.19			
		SES	-7.95	3.55	-0.28			
		Bedtime Resistance	-1.59	0.97	-0.29			
		Sleep Onset Delay	***8.71***	***3.19***	***0.37****			
		Sleep Duration	5.40	1.47	0.49			
		Sleep Anxiety	0.29	1.06	0.04			
		Night Wakings	0.77	1.54	0.08			
		Parasomnia	0.51	0.66	0.10			
		Sleep Disordered Breathing	-0.91	1.18	-0.10			
		Daytime Sleepiness	***1.64***	***0.60***	***0.33****			
FASD	1	(Constant)	22.82	1.81		0.00	0.12	0.00
n=105		Age	-0.01	0.01	-0.05			
		Sex	-0.73	0.72	-0.10			
		SES	-1.26	0.61	-0.20			
	2	(Constant)	12.40	2.73		0.35	6.94	**0.40****
		Age	0.00	0.01	-0.04			
		Sex	-0.46	0.62	-0.06			
		SES	-0.63	0.54	-0.10			
		Bedtime Resistance	-0.25	0.16	-0.22			
		Sleep Onset Delay	0.84	0.52	0.16			
		Sleep Duration	0.38	0.19	0.20			
		Sleep Anxiety	***0.47***	***0.16***	***0.38****			
		Night Wakings	-0.11	0.21	-0.06			
		Parasomnia	***0.40***	***0.11***	***0.40****			
		Sleep Disordered Breathing	-0.07	0.19	-0.04			
		Daytime Sleepiness	-0.05	0.11	-0.04			
TD	1	(Constant)	13.28	2.58		0.00	0.02	0.00
n=101		Age	0.00	0.02	0.00			
		Sex	-1.14	0.91	-0.13			
		SES	-0.20	0.78	-0.03			
	2	(Constant)	7.07	3.68		0.15	1.96	0.16
		Age	-0.01	0.02	-0.08			
		Sex	-0.44	0.90	-0.05			
		SES	0.36	0.82	0.05			
		Bedtime Resistance	-0.27	0.22	-0.18			
		Sleep Onset Delay	-0.76	0.71	-0.13			
		Sleep Duration	0.61	0.33	0.22			
		Sleep Anxiety	0.44	0.29	0.23			
		Night Wakings	-0.20	0.38	-0.06			
		Parasomnia	0.31	0.17	0.21			
		Sleep Disordered Breathing	0.06	0.35	0.02			
		Daytime Sleepiness	0.17	0.15	0.14			

***p=<0.05, ** p=<0.001.**

2.7.3 Sleep as a predictor of Planning and Organising

Sleep disturbances were associated with Planning and Organising in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Planning and Organising and CSHQ variables are presented in Table 2.16. In the Autism group, composite sleep scores were significant predictors of Planning and Organising (ΔR^2 = 0.34, $\Delta F_{(1,55)}$ =3.35, p = <0.001), as well as the subscale of Sleep Duration (**ß** = 0.52, p=<0.001. In the FASD group, composite sleep scores were significant predictors of Planning and Organising (ΔR^2 = 0.22, $\Delta F_{(1,105)}$ =3.93, p = <0.001), as well as the subscales of Sleep Duration (**ß** = 0.25, p= 0.02) and Parasomnia (**ß** = 0.35, p= <0.001). In the TD group, composite sleep scores were significant predictors of Planning and Organising (ΔR^2 = 0.18, $\Delta F_{(1,101)}$ =2.72, p = 0.01), as well as the subscales of Sleep Duration (**ß** = 0.25, p= 0.03) and Sleep Anxiety (**ß** = 0.37, p= 0.01). Sleep disturbances explained 43% of the variance in SCAS Total scores in the Autism group, 33% in the FASD group and 25% in the TD group after controlling for age, SES and sex.

Group comparisons in Planning and Organising

Raw Score: Overall, the tests of between subject effects on the Planning and Organising subscale showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=43.82, p=<0.001, R^2=0.25). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher) and significant similarities between the FASD and Autism group when using the range of acceptability of 10% (p=<0.05; both scoring very similarly). *Sex*: There were significant differences between Autism and FASD boys and girls, with girls scoring higher than boys in both groups (Autism: Fem: m=32.67 SD=16.99; Male: m=23.61, SD=5.98 conditions t(56)=1.869, p=0.03. FASD: Fem: m=29.72 SD=6.69; Male: m=17.51, SD=5.42 conditions t(105)=0.878, p=0.02). Age and SES were not significant predictors of Planning and Organising in any of the groups.

Table 2.16: Hierarchical multiple regression results for BRIEF Subscale Planning and Organising

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	45.18	9.98		0.01	0.47	0.01
n= 68		Age	-0.04	0.07	-0.08			
		Sex	-8.43	4.94	-0.22			
		SES	-4.13	3.20	-0.17			
	2	(Constant)	49.10	13.96		0.34	3.35	**0.43****
		Age	0.01	0.06	0.01			
		Sex	-7.41	4.67	-0.20			
		SES	-6.69	3.22	-0.28			
		Bedtime Resistance	-1.20	0.88	-0.26			
		Sleep Onset Delay	-6.67	2.89	-0.33			
		Sleep Duration	***4.79***	***1.34***	***0.52****			
		Sleep Anxiety	-0.09	0.96	-0.02			
		Night Wakings	0.69	1.40	0.08			
		Parasomnia	0.56	0.60	0.13			
		Sleep Disordered Breathing	-0.95	1.07	-0.12			
		Daytime Sleepiness	-0.71	0.55	-0.17			
FASD	1	(Constant)	28.51	2.45		0.04	4.23	**0.04***
n=105		Age	0.02	0.01	0.11			
		Sex	-0.68	0.98	-0.07			
		SES	-0.37	0.82	-0.04			
	2	(Constant)	15.84	3.85		0.22	3.93	**0.33****
		Age	0.02	0.01	0.12			
		Sex	-0.45	0.87	-0.05			
		SES	0.52	0.76	0.06			
		Bedtime Resistance	-0.47	0.22	-0.32			
		Sleep Onset Delay	-0.13	0.74	-0.02			
		Sleep Duration	***0.64***	***0.27***	***0.25****			
		Sleep Anxiety	0.84	0.23	0.05			
		Night Wakings	-0.07	0.29	-0.03			
		Parasomnia	***0.46***	***0.15***	***0.35****			
		Sleep Disordered Breathing	-0.10	0.26	-0.04			
		Daytime Sleepiness	0.01	0.16	0.01			
TD	1	(Constant)	20.73	3.55		0.03	2.62	0.03
n=101		Age	0.01	0.02	0.06			
		Sex	-3.61	1.25	-0.28			
		SES	-0.51	1.07	-0.05			
	2	(Constant)	9.84	4.81		0.18	2.72	**0.25***
		Age	0.00	0.02	-0.02			
		Sex	-2.47	1.18	-0.20			
		SES	0.14	1.07	0.01			
		Bedtime Resistance	-0.63	0.29	-0.30			
		Sleep Onset Delay	-0.94	0.92	-0.12			
		Sleep Duration	***0.98***	***0.44***	***0.25****			
		Sleep Anxiety	***1.01***	***0.38***	***0.37****			
		Night Wakings	0.26	0.50	0.05			
		Parasomnia	0.32	0.22	0.15			
		Sleep Disordered Breathing	0.30	0.46	0.07			
		Daytime Sleepiness	0.20	0.20	0.12			

******p*=<0.05, ** *p*=<0.001.**

2.7.4 Sleep as a predictor of Organising Materials

Sleep disturbances were associated with Organising Materials in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Organising Materials and CSHQ variables are presented in Table 2.17. In the Autism group, composite sleep scores were significant predictors of Organising Materials (ΔR^2 = 0.40, $\Delta F_{(1,55)}$ =4.48, p = <0.001), as well as the subscale of Sleep Onset Delay (**ß** =0.43, p=0.03) and Sleep Duration (**ß** = 0.47, p=<0.001). In the FASD group, composite sleep scores were significant predictors of Organising Materials (ΔR^2 = 0.20, $\Delta F_{(1,105)}$ =3.01, p = <0.001), as well as the subscale of Sleep Anxiety (**ß** = 0.56, p= <0.001). In the TD group, composite sleep scores were not significant predictors of Organising Materials (ΔR^2 = 0.09, $\Delta F_{(1,101)}$ =1.15, p = 0.35), and neither were subscales. Sleep disturbances explained 49% of the variance in Organising Materials scores in the Autism group, 22% in the FASD group and 15% (non-significant result) in the TD group after controlling for age, SES and sex.

Group comparisons in Organising Materials

Raw Score: Overall, the tests of between subject effects on the Organising Materials subscale showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=17.38, p=<0.001, R^2=0.25). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher), TD/FASD (p=<0.001; FASD group scoring higher), and Autism/FASD groups (p=0.02; Autism group scoring higher). *SES*: There were significant SES differences in the TD group with the lower SES group scoring higher than higher SES group ($F_{(2, 101)}$=3.29, p=0.04, R^2=0.06). Sex: There were no significant differences between Autism boys and girls, with girls scoring significantly higher than boys (Fem: m=20.04 SD=16.98; Male: m=12.769, SD=2.95 conditions t(56)=1.56, p=0.05). Age was not a predictor of Organising Materials in any of the groups.

Table 2.17: Hierarchical multiple regression results for BRIEF Subscale Organising Materials

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	35.90	9.54		0.03	1.47	0.03
n= 68		Age	-0.07	0.06	-0.15			
		Sex	-6.64	4.72	-0.19			
		SES	-3.88	3.06	-0.17			
	2	(Constant)	47.96	12.41		0.40	4.48	**0.49****
		Age	0.00	0.06	0.00			
		Sex	-6.63	4.15	-0.19			
		SES	-8.08	2.86	-0.35			
		Bedtime Resistance	-1.00	0.78	-0.22			
		Sleep Onset Delay	***8.35***	***2.57***	***0.43****			
		Sleep Duration	***4.20***	***1.19***	***0.47****			
		Sleep Anxiety	0.24	0.85	0.05			
		Night Wakings	1.27	1.24	0.16			
		Parasomnia	-0.02	0.53	-0.01			
		Sleep Disordered Breathing	-0.90	0.95	-0.12			
		Daytime Sleepiness	-0.87	0.49	-0.22			
FASD	1	(Constant)	15.44	1.55		0.01	0.87	0.01
n=105		Age	0.01	0.01	0.09			
		Sex	0.01	0.62	0.00			
		SES	-0.83	0.52	-0.16			
	2	(Constant)	10.35	2.62		0.20	3.01	**0.22***
		Age	0.01	0.01	0.14			
		Sex	0.03	0.59	0.01			
		SES	-0.53	0.52	-0.10			
		Bedtime Resistance	-0.21	0.15	-0.22			
		Sleep Onset Delay	-0.05	0.50	-0.01			
		Sleep Duration	0.30	0.18	0.18			
		Sleep Anxiety	***0.59***	***0.16***	***0.56****			
		Night Wakings	-0.20	0.20	-0.11			
		Parasomnia	-0.04	0.10	-0.05			
		Sleep Disordered Breathing	-0.12	0.18	-0.07			
		Daytime Sleepiness	0.14	0.11	0.14			
TD	1	(Constant)	10.15	2.58		0.00	0.34	0.00
n=101		Age	0.00	0.02	0.00			
		Sex	-1.97	0.91	-0.21			
		SES	0.92	0.78	0.12			
	2	(Constant)	9.83	3.81		0.09	1.15	0.15
		Age	-0.01	0.02	-0.07			
		Sex	-1.54	0.93	-0.17			
		SES	0.77	0.84	0.10			
		Bedtime Resistance	-0.43	0.23	-0.28			
		Sleep Onset Delay	0.20	0.73	0.03			
		Sleep Duration	0.51	0.35	0.18			
		Sleep Anxiety	0.39	0.30	0.20			
		Night Wakings	0.28	0.40	0.08			
		Parasomnia	-0.17	0.17	-0.11			
		Sleep Disordered Breathing	0.21	0.37	0.06			
		Daytime Sleepiness	0.01	0.16	0.01			

***p*=<0.05, ** *p*=<0.001.**

2.7.5 Sleep as a predictor of Inhibition

Sleep disturbances were associated with Inhibition in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Inhibition and CSHQ variables are presented in Table 2.18. In the Autism group, composite sleep scores were significant predictors of Inhibition (ΔR^2 = 0.34, $\Delta F_{(1,55)}$ =3.41, p = <0.001), as well as the subscale of Sleep Duration (**ß** = 0.50, p=0.03). In the FASD group, composite sleep scores were significant predictors of Inhibition (ΔR^2 = 0.31, $\Delta F_{(1,105)}$ =5.32, p = <0.001), as well as the subscales of Bedtime Resistance (**ß** = 0.36, p= 0.02) and Sleep Duration (**ß** = 0.29, p= 0.01). In the TD group, composite sleep scores were significant predictors of Inhibition (ΔR^2= 0.19, $\Delta F_{(1,101)}$ =2.93, p = 0.01), and subscale of Bedtime Resistance (**ß** =0.28, p= 0.05). Sleep disturbances explained 44% of the variance in Inhibition in the Autism group, 32% in the FASD group and 26% in the TD group after controlling for age, SES and sex.

Group comparisons in Inhibition

Raw Score: Overall, the tests of between subject effects on the Inhibition subscale showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=33.97, p=<0.001, R^2=0.20). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher) but no similarities or differences between the Autism/ FASD groups. *Sex*: There were significant differences between Autism, FASD and TD boys and girls, with girls scoring higher than boys in all three groups (Autism Fem: m= 28.08 SD=17.98; Male: m=19.62, SD=3.89 conditions t(56)=1.70, p=0.01. FASD Fem: m= 23.88 SD=3.21; Male: m=23.12, SD=5.02 conditions t(105)=0.94, p=0.02. TD Fem: m= 23.88 SD=3.21; Male: m=23.12, SD=5.02 conditions t(105)=0.94, p=0.02). Age and SES were not significant predictors of Inhibition in any of the groups.

Table 2.18: Hierarchical multiple regression results for BRIEF Subscale Inhibition

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	44.47	10.20		0.03	1.49	0.03
n= 68		Age	-0.08	0.07	-0.15			
		Sex	-7.85	5.05	-0.20			
		SES	-3.77	3.27	-0.15			
	2	(Constant)	53.55	14.04		0.34	3.41	**0.44****
		Age	-0.02	0.07	-0.05			
		Sex	-6.83	4.69	-0.18			
		SES	-6.76	3.24	-0.27			
		Bedtime Resistance	-1.31	0.88	-0.27			
		Sleep Onset Delay	-6.64	2.91	-0.32			
		Sleep Duration	***4.71***	***1.34***	***0.50****			
		Sleep Anxiety	0.09	0.97	0.02			
		Night Wakings	0.74	1.41	0.09			
		Parasomnia	0.35	0.60	0.08			
		Sleep Disordered Breathing	-0.92	1.08	-0.12			
		Daytime Sleepiness	-0.97	0.55	-0.22			
FASD	1	(Constant)	24.44	2.06		0.00	0.00	0.00
n=105		Age	0.00	0.01	-0.01			
		Sex	-0.77	0.82	-0.09			
		SES	-0.20	0.69	-0.03			
	2	(Constant)	14.17	3.23		0.31	5.32	**0.32****
		Age	0.00	0.01	-0.01			
		Sex	-0.62	0.73	-0.08			
		SES	0.51	0.64	0.07			
		Bedtime Resistance	***0.44***	***0.19***	***0.36****			
		Sleep Onset Delay	0.18	0.62	0.03			
		Sleep Duration	0.62	0.23	**0.29***			
		Sleep Anxiety	0.70	0.19	0.50			
		Night Wakings	-0.20	0.25	-0.09			
		Parasomnia	0.42	0.13	0.38			
		Sleep Disordered Breathing	-0.17	0.22	-0.08			
		Daytime Sleepiness	0.09	0.13	0.07			
TD	1	(Constant)	19.09	3.14		0.00	0.16	0.00
n=101		Age	0.00	0.02	-0.02			
		Sex	-2.66	1.11	-0.24			
		SES	-0.81	0.95	-0.09			
	2	(Constant)	10.38	4.34		0.19	2.93	**0.26***
		Age	-0.03	0.02	-0.15			
		Sex	-1.67	1.06	-0.15			
		SES	-0.64	0.96	-0.07			
		Bedtime Resistance	***0.52***	***0.26***	***0.28****			
		Sleep Onset Delay	0.41	0.83	0.06			
		Sleep Duration	0.48	0.39	0.14			
		Sleep Anxiety	0.41	0.35	0.17			
		Night Wakings	0.60	0.45	0.13			
		Parasomnia	0.35	0.20	0.19			
		Sleep Disordered Breathing	0.42	0.42	0.11			
		Daytime Sleepiness	0.20	0.18	0.13			

***p*=<0.05, ** *p*=<0.001.**

2.7.6 Sleep as a predictor of Initiation

Sleep disturbances were associated with Initiation in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Initiation and CSHQ variables are presented in Table 2.19. In the Autism group, composite sleep scores were significant predictors of Initiation (ΔR^2 = 0.37, $\Delta F_{(1,55)}$ =3.96, p = <0.001), as well as the subscale of Sleep Duration (**ß** = 0.43, p=<0.001). In the FASD group, composite sleep scores were significant predictors of Initiation (ΔR^2 = 0.24, $\Delta F_{(1,105)}$ =3.97, p=<0.001), as well as the subscale of Sleep Anxiety (**ß** = 0.54, p= <0.001). There were no significant regressions in the TD group. Sleep disturbances explained 48% of the variance Initiation in the Autism group, 28% in the FASD group and 16% (non-significant result) in the TD group after controlling for age, SES and sex.

Group comparisons in Initiation

Raw Score: Overall, the tests of between subject effects on the Initiation subscale showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=25.23, p=<0.001, R^2=0.16). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher) but no significant differences or similarities between the FASD/ Autism groups. *SES*: There were significant SES differences in the FASD group with lower SES scoring higher than higher SES ($F_{(2, 104)}$=3.46, p=0.04, R^2=0.07). *Sex*: There were significant differences between Autism boys and girls, with girls scoring higher than boys (Fem: m=25.33 SD=18.99; Male: m=15.76, SD=3.67 conditions t(56)=1.78, p=0.01). Age was not a significant predictor of Initiation in any of the groups.

Table 2.19: Hierarchical multiple regression results BRIEF Subscale Initiation

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	43.98	10.99		0.03	1.70	0.03
n= 68		Age	-0.09	0.07	-0.16			
		Sex	-8.86	5.43	-0.21			
		SES	-4.21	3.53	-0.16			
	2	(Constant)	60.43	14.67		0.37	3.96	**0.48****
		Age	-0.02	0.07	-0.03			
		Sex	-8.54	4.90	-0.21			
		SES	-8.81	3.39	-0.33			
		Bedtime Resistance	-1.41	0.92	-0.27			
		Sleep Onset Delay	-8.30	3.04	-0.37			
		Sleep Duration	***4.43***	***1.40***	***0.43****			
		Sleep Anxiety	0.25	1.01	0.04			
		Night Wakings	1.62	1.47	0.18			
		Parasomnia	-0.10	0.63	-0.02			
		Sleep Disordered Breathing	-0.85	1.13	-0.10			
		Daytime Sleepiness	-1.08	0.58	-0.23			
FASD	1	(Constant)	19.83	1.57		0.01	0.88	0.01
n=105		Age	0.01	0.01	0.08			
		Sex	-0.67	0.63	-0.11			
		SES	-0.74	0.53	-0.14			
	2	(Constant)	11.49	2.57		0.24	3.97	**0.28****
		Age	0.01	0.01	0.12			
		Sex	-0.43	0.58	-0.07			
		SES	-0.11	0.51	-0.02			
		Bedtime Resistance	-0.28	0.15	-0.30			
		Sleep Onset Delay	-0.13	0.49	-0.03			
		Sleep Duration	0.24	0.18	0.15			
		Sleep Anxiety	***0.58***	***0.15***	***0.54****			
		Night Wakings	-0.16	0.20	-0.09			
		Parasomnia	0.19	0.10	0.23			
		Sleep Disordered Breathing	0.07	0.18	0.04			
		Daytime Sleepiness	0.14	0.10	0.14			
TD	1	(Constant)	12.49	2.77		0.00	0.04	0.00
n=101		Age	0.01	0.02	0.06			
		Sex	-2.00	0.98	-0.21			
		SES	0.33	0.84	0.04			
	2	(Constant)	6.46	4.00		0.12	1.61	0.16
		Age	0.00	0.02	0.00			
		Sex	-1.40	0.98	-0.14			
		SES	0.69	0.89	0.08			
		Bedtime Resistance	-0.40	0.24	-0.25			
		Sleep Onset Delay	-0.16	0.77	-0.03			
		Sleep Duration	0.25	0.36	0.08			
		Sleep Anxiety	0.62	0.32	0.30			
		Night Wakings	0.26	0.42	0.07			
		Parasomnia	0.07	0.18	0.04			
		Sleep Disordered Breathing	0.47	0.38	0.14			
		Daytime Sleepiness	0.13	0.16	0.09			

***p=<0.05, ** p=<0.001.**

2.7.7 Sleep as a predictor of Emotional Control

Sleep disturbances were associated with Emotional Control in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Emotional Control and CSHQ variables are presented in Table 2.20. In the Autism group, composite sleep scores were significant predictors of Emotional Control (ΔR^2 = 0.35, $\Delta F_{(1,55)}$ =3.41, p = <0.001), as well as the subscale of Sleep Duration (**ß** = 0.52, p=<0.001). In the FASD group, composite sleep scores were significant predictors of SCAS Total score (ΔR^2 = 0.23, $\Delta F_{(1,105)}$ =3.48, p = <0.001), as well as the subscales of Sleep Duration (**ß** = 0.28, p= 0.01) and Sleep Anxiety (**ß** = 0.37, p= 0.01). In the TD group, composite sleep scores were significant predictors of Emotional Control (ΔR^2 = 0.17, $\Delta F_{(1,101)}$ =2.46, p = 0.02), And the Subscale of Sleep Duration (**ß** = 0.26, p= 0.03). Sleep disturbances explained 43% of the variance in Emotional Control in the Autism group, 23% in the FASD group and 21% in the TD group after controlling for age, SES and sex.

Group comparisons in Emotional Control

Raw Score: Overall, the tests of between subject effects on the Emotional Control subscale showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=40.07, p=<0.001, R^2=0.23). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001 Autism group scoring higher), TD/FASD groups (p=<0.001; FASD group scoring higher) and Autism/FASD (p=0.01; Autism group scoring higher). *Sex*: There were significant differences between FASD boys and girls, with girls scoring higher than boys (Fem: m=26.93 SD=4.07; Male: m=26.53, SD=4.96 conditions t(105)=0.459, p=0.03). Age and SES were not significant predictors of Emotional control in any of the groups.

Table 2.20: Hierarchical multiple regression results for BRIEF Subscale Emotional Control

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	42.97	9.49		0.01	0.33	0.01
n= 68		Age	-0.03	0.06	-0.06			
		Sex	-5.67	4.69	-0.16			
		SES	-4.52	3.05	-0.20			
	2	(Constant)	49.73	13.06		0.35	3.41	**0.43****
		Age	0.03	0.06	0.05			
		Sex	-5.03	4.36	-0.14			
		SES	-7.02	3.01	-0.31			
		Bedtime Resistance	-1.21	0.82	-0.27			
		Sleep Onset Delay	-6.93	2.70	-0.37			
		Sleep Duration	***4.58***	***1.25***	***0.52****			
		Sleep Anxiety	0.55	0.90	0.11			
		Night Wakings	0.04	1.31	0.01			
		Parasomnia	0.40	0.56	0.10			
		Sleep Disordered Breathing	-0.92	1.00	-0.13			
		Daytime Sleepiness	-0.86	0.51	-0.22			
FASD	1	(Constant)	27.25	2.23		0.00	0.22	0.00
n=105		Age	0.01	0.01	0.04			
		Sex	-0.34	0.89	-0.04			
		SES	-0.52	0.75	-0.07			
	2	(Constant)	20.30	3.71		0.23	3.48	**0.23****
		Age	0.01	0.01	0.06			
		Sex	-0.40	0.84	-0.04			
		SES	-0.25	0.73	-0.03			
		Bedtime Resistance	-0.12	0.21	-0.09			
		Sleep Onset Delay	0.18	0.71	0.03			
		Sleep Duration	***0.65***	***0.26***	***0.28****			
		Sleep Anxiety	***0.56***	***0.22***	***0.37****			
		Night Wakings	-0.49	0.28	-0.20			
		Parasomnia	0.22	0.15	0.19			
		Sleep Disordered Breathing	0.03	0.25	0.01			
		Daytime Sleepiness	-0.09	0.15	-0.06			
TD	1	(Constant)	19.90	3.65		0.00	0.08	0.00
n=101		Age	0.01	0.02	0.04			
		Sex	-2.38	1.29	-0.19			
		SES	-0.64	1.11	-0.06			
	2	(Constant)	10.12	5.12		0.17	2.46	**0.21***
		Age	-0.02	0.02	-0.08			
		Sex	-1.20	1.26	-0.09			
		SES	0.36	1.14	0.03			
		Bedtime Resistance	-0.37	0.31	-0.18			
		Sleep Onset Delay	-0.85	0.98	-0.11			
		Sleep Duration	***1.04***	***0.46***	***0.26****			
		Sleep Anxiety	0.56	0.41	0.20			
		Night Wakings	-0.32	0.53	-0.06			
		Parasomnia	0.28	0.23	0.13			
		Sleep Disordered Breathing	0.39	0.49	0.09			
		Daytime Sleepiness	0.36	0.21	0.20			

***p*=<0.05, ** *p*=<0.001**

2.7.8 Sleep as a predictor of Executive Functioning

Sleep disturbances were associated with Total BRIEF in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Total BRIEF and CSHQ variables are presented in table 2.21. In the Autism group, composite sleep scores were significant predictors of Total BRIEF (ΔR^2 = 0.23, $\Delta F_{(1,55)}$ =1.91, p = 0.05), as well as the subscale of Sleep Duration (**ß** =0.35, p=0.03) and Parasomnia (**ß** = 0.42, p=0.01). In the FASD group, composite sleep scores were significant predictors of BRIEF Total Score (ΔR^2 = 0.33, $\Delta F_{(1,105)}$ =6.11, p = <0.001), as well as the subscales of Sleep Duration (**ß** = 0.28, p= 0.01), Sleep Anxiety (**ß** = 0.50, p= <0.001) and Parasomnia (**ß** =0.34, p= <0.001). In the TD group, composite sleep scores were significant predictors of BRIEF Total Score (ΔR^2 = 0.29, $\Delta F_{(1,101)}$ =5.19, p=<0.001), as well as the subscales of Bedtime Resistance (**ß**=0.26, p= 0.05), Sleep Duration (**ß**=0.34, p=<0.001), Sleep Anxiety (**ß** =0.33, p=0.02), Parasomnia (**ß**=0.20, p=0.04) and Daytime Sleepiness (**ß** =0.23, p=0.04). Sleep disturbances explained 31% of the variance in SCAS Total scores in the Autism group, 36% in the FASD group and 36% in the TD group after controlling for age, SES and sex.

Group comparisons in Total BRIEF

Raw Score: Overall, the tests of between subject effects on the Total BRIEF showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=97.49, p=<0.001, R^2=0.42). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001) but no significant similarities or differences between the FASD/ Autism groups. *SES*: There were no significant SES differences in the FASD group. *Sex*: There were no significant differences groups. *Age*: There were no significant overall age differences in the Autism, FASD or TD groups.

Table 2.21: Hierarchical multiple regression results for Total BRIEF

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	138.95	23.02		0.05	2.78	0.05
n= 68		Age	0.27	0.16	0.23			
		Sex	-10.79	11.38	-0.13			
		SES	-5.18	7.38	-0.09			
	2	(Constant)	62.86	34.68		0.23	1.91	**0.31***
		Age	0.24	0.16	0.21			
		Sex	-8.24	11.59	-0.10			
		SES	-0.44	8.00	-0.01			
		Bedtime Resistance	1.08	2.18	0.10			
		Sleep Onset Delay	5.47	7.18	0.12			
		Sleep Duration	***7.52***	***3.32***	***0.35****			
		Sleep Anxiety	0.72	2.39	0.06			
		Night Wakings	-2.19	3.48	-0.12			
		Parasomnia	***4.18***	***1.48***	***0.42****			
		Sleep Disordered Breathing	0.81	2.67	0.05			
		Daytime Sleepiness	1.10	1.36	0.11			
FASD	1	(Constant)	184.04	13.12		0.01	0.78	0.01
n=105		Age	0.06	0.08	0.07			
		Sex	5.02	5.24	0.09			
		SES	5.62	4.41	0.12			
	2	(Constant)	113.73	20.17		0.33	6.11	**0.36****
		Age	0.07	0.07	0.09			
		Sex	3.98	4.56	0.08			
		SES	1.37	3.97	0.03			
		Bedtime Resistance	2.11	1.16	0.27			
		Sleep Onset Delay	1.15	3.86	0.03			
		Sleep Duration	***3.89***	***1.42***	***0.28****			
		Sleep Anxiety	***4.50***	***1.21***	***0.50****			
		Night Wakings	1.74	1.53	0.12			
		Parasomnia	***2.36***	***0.79***	***0.34****			
		Sleep Disordered Breathing	0.53	1.38	0.04			
		Daytime Sleepiness	0.20	0.82	0.02			
TD	1	(Constant)	123.86	19.15		0.01	0.94	0.01
n=101		Age	0.11	0.11	0.11			
		Sex	-15.63	6.75	-0.23			
		SES	-6.32	5.80	-0.11			
	2	(Constant)	53.06	24.53		0.29	5.19	**0.36****
		Age	-0.01	0.11	-0.01			
		Sex	-8.14	6.01	-0.12			
		SES	0.21	5.44	0.00			
		Bedtime Resistance	***2.97***	***1.47***	***0.26****			
		Sleep Onset Delay	-10.14	4.70	-0.03			
		Sleep Duration	***7.21***	***2.22***	***0.34****			
		Sleep Anxiety	***4.87***	***1.96***	***0.33****			
		Night Wakings	0.04	2.56	0.00			
		Parasomnia	***2.29***	***1.11***	***0.20****			
		Sleep Disordered Breathing	1.44	2.35	0.06			
		Daytime Sleepiness	***2.13***	***1.01***	***0.23****			

***p*=<0.05, ** *p*=<0.001.**

2.7.9 Summary

Children with FASD and Autism scored consistently higher than the TD group in every BRIEF subscale. Children in the Autism group consistently scored higher than children with FASD. Syndrome specificity (occasions where there were significant differences between all three groups) were noted in the subscales of Shifting, Organisation of Materials, Monitoring and Emotional Control. There were no significantly similar raw scores.

There were sex related differences in executive functioning scores. In the Autism group, boys scored significantly higher than girls in the subscales of Working Memory and Planning and Organising. Meanwhile girls scored significantly higher than boys in the subscales of Organisation of Materials, Monitoring, Inhibition, Initiation and Total BRIEF. In the FASD group, girls scored significantly higher than boys in the subscales of Planning and Organising, Monitoring, Inhibition and Emotional Control. In the TD group, girls scored significantly higher in the subscales of Shifting, Monitoring, and Inhibition. TD girls and girls with FASD tended to score higher than boys, but girls and boys in the Autism sample had more variations in their scores.

SES correlated with executive functioning scores. Scores on Working Memory and Shifting in the FASD group, and Organisation of Materials in the TD group were significantly higher in lower SES groups.

Executive functioning scores were significantly associated with sleep problems in all three groups. In the Autism group, Sleep Duration accounted for the largest amount of variance in BRIEF subscales; in total, sleep problems predicted 31% of the variance in BRIEF scores. In the FASD group, Sleep Duration, Sleep Anxiety and Parasomnias accounted for the largest amount of variance in the BRIEF subscales; in total, sleep problems predicted 36% of variance in the BRIEF scores. In the TD group, Sleep Duration,

Bedtime Resistance and Sleep Anxiety were the biggest predictors of BRIEF subscales; in total, sleep problems predicted 36% of the variance in BRIEF scores.

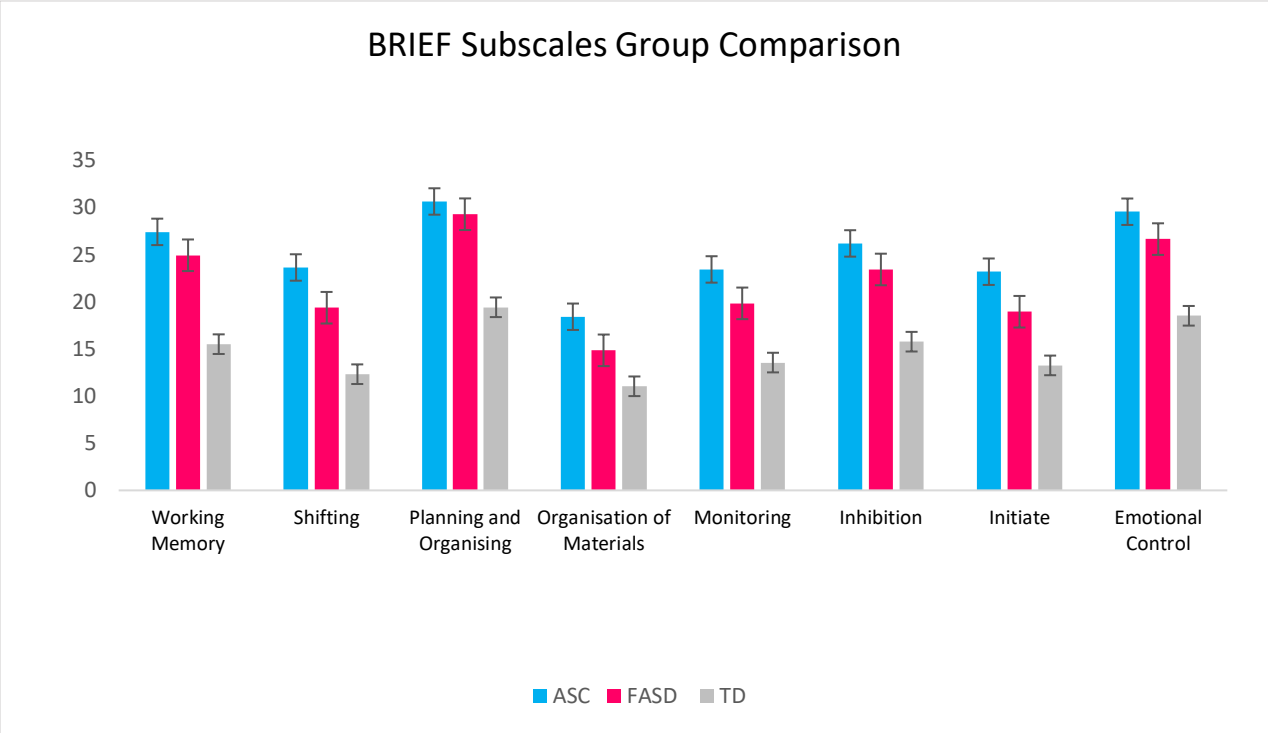


Figure 2.5: Comparison between Autism, FASD and TD scores on the BRIEF subscales (SE bars)

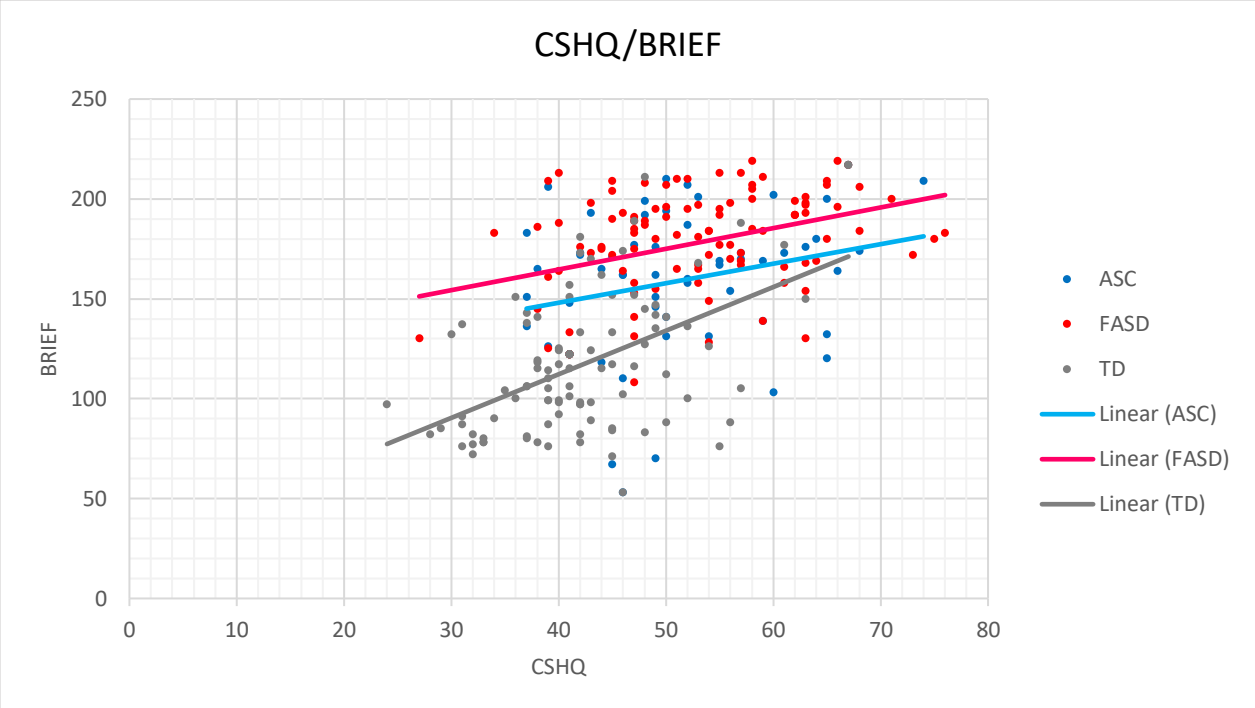


Figure 2.6: Scatter plot showing raw scores: sleep (CSHQ) against executive functioning (BRIEF)

2.8 Results: Child Behaviour Checklist (CBCL)

The following section provides an overview of the behavioural profiles of children with FASD and Autism. As noted above, behaviour is the result of a complex interaction between executive functions, environmental stimuli and emotional responses. For those working with children with FASD, there appear to be more clinical and educational resources for externalised, aggressive and conduct related behaviours than internalised or withdrawn behaviours – most probably because the externalised behaviours warrant more immediate responses from caregivers and educators. For this reason, much of what has been researched on FASD and behaviour has focussed on externalised behaviours.

The CBCL variables were analysed using group mean comparisons. ANOVA results are presented in Table 2.22. Hierarchical multiple regression analyses were conducted to examine the associations between each BRIEF subscale and CSHQ subscale. These are presented in tables 2.23 – 2.31.

Table 2.22: Mean Scores (SD) and group differences using ANOVA for CBCL subsets

	Autism (n=61)		FASD (n=114)		TD (n=104)		F	*p*	ηp2
	m	sd	m	sd	m	sd			
Withdrawn [i]	5.81	3.42	6.17	3.75	3.22	3.20	21.04	<0.001	0.14
Somatic [i]	3.93	3.23	4.49	3.19	2.34	2.89	13.26	<0.001	0.09
Anxious [i]	11.55	5.84	12.24	6.24	7.00	6.94	19.36	<0.001	0.13
Social [i]	6.05	2.79	7.54	3.14	2.48	2.37	89.31	<0.001	0.40
Thought [i]	4.62	2.82	4.98	2.83	1.68	2.14	48.27	<0.001	0.27
Attention [e]	10.57	4.10	12.63	3.96	4.65	3.87	111.61	<0.001	0.46
Delinquency [e]	3.86	3.31	7.07	4.45	2.95	3.47	32.11	<0.001	0.20
Aggression [e]	15.72	8.61	22.80	9.14	10.44	9.23	49.13	<0.001	0.27
Total	**62.21**	**22.67**	**77.90**	**25.81**	**34.76**	**28.84**	**71.02**	**<0.001**	**0.35**

[i] *internalising* [e] *externalising*

2.8.1 Sleep as a predictor of Withdrawn

Sleep disturbances significantly associated with Withdrawn symptomology in the Autism, and TD groups. Hierarchical multiple regression results examining the associations between Withdrawn and CSHQ variables are presented in Table 2.23. In the Autism group, composite sleep scores were significant predictors of Withdrawn (ΔR^2 = 0.13, $\Delta F_{(1,55)}$ =1.00, p = 0.001). In the TD group, composite sleep scores were significant predictors of Withdrawn (ΔR^2 = 0.21, $\Delta F_{(1,101)}$ =3.54, p = 0.001), as well as the subscales of Bedtime Resistance (**ß** = 0.25, p= 0.01) and Daytime Sleepiness (**ß** =0.39, p=<0.001). Sleep disturbances explained 26% of the variance in Withdrawn scores in the Autism group, 17% (non-significant result) in the FASD group and 34% in the TD group after controlling for age, SES and sex.

Group comparisons in Withdrawn

Raw Score: Overall, the tests of between subject effects on the Withdrawn subscale showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=21.04, p=<0.001, R^2=0.14). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher), and significant similarities between the FASD/ Autism groups when using the range of acceptability of 10% (p=<0.05). *Sex*: There were significant differences in the Autism group between girls and boys, with boys scoring significantly higher than girls (Fem: m=5.73 SD=3.59; Male: m=6.08, SD=2.84 conditions t(56)=-0.316, p=0.03). *Age*: There were significant age related associations in the Autism, FASD and TD groups with older children scoring significantly higher than younger children (Autism: $F_{(1,56)}$=8.52, p=0.01, R^2=0.13; FASD: $F_{(1,105)}$=9.42, p=0.003, R^2=0.08, $F_{(1,103)}$=12.23, p=0.001, R^2=0.11). SES was not a significant predictor of Withdrawn symptomology in any of the groups.

Table 2.23: Hierarchical multiple regression results for CBCL subscale Withdrawn

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	0.92	2.13		0.13	8.37	**0.13***
n= 68		Age	0.04	0.01	0.36			
		Sex	0.30	1.05	0.04			
		SES	-0.02	0.68	0.00			
	2	(Constant)	-5.32	3.42		0.13	1.00	**0.26***
		Age	0.03	0.02	0.25			
		Sex	0.36	1.14	0.04			
		SES	0.77	0.79	0.15			
		Bedtime Resistance	0.11	0.22	-0.11			
		Sleep Onset Delay	0.61	0.71	0.14			
		Sleep Duration	0.54	0.33	0.27			
		Sleep Anxiety	0.14	0.24	0.11			
		Night Wakings	0.21	0.34	0.12			
		Parasomnia	0.05	0.15	0.05			
		Sleep Disordered Breathing	0.14	0.26	0.08			
		Daytime Sleepiness	0.26	0.13	0.28			
FASD	1	(Constant)	2.13	1.79		0.08	9.42	0.08
n= 102		Age	0.03	0.01	0.29			
		Sex	0.14	0.72	0.02			
		SES	0.08	0.60	0.01			
	2	(Constant)	-2.32	3.23		0.09	1.21	0.17
		Age	0.03	0.01	0.28			
		Sex	0.30	0.73	0.04			
		SES	0.17	0.64	0.03			
		Bedtime Resistance	0.19	0.19	-0.17			
		Sleep Onset Delay	0.61	0.62	0.12			
		Sleep Duration	0.35	0.23	0.18			
		Sleep Anxiety	0.27	0.19	0.21			
		Night Wakings	-0.35	0.25	-0.17			
		Parasomnia	0.03	0.13	0.03			
		Sleep Disordered Breathing	0.32	0.22	0.16			
		Daytime Sleepiness	0.07	0.13	0.06			
TD	1	(Constant)	0.94	1.73		0.11	12.11	0.11
n= 101		Age	0.03	0.01	0.32			
		Sex	-0.69	0.61	-0.11			
		SES	-0.58	0.52	-0.11			
	2	(Constant)	-5.09	2.34		0.21	3.54	**0.34***
		Age	0.02	0.01	0.16			
		Sex	-0.10	0.57	-0.02			
		SES	0.08	0.52	0.02			
		Bedtime Resistance	0.10	0.14	0.09			
		Sleep Onset Delay	0.21	0.45	0.05			
		Sleep Duration	0.04	0.21	0.02			
		Sleep Anxiety	0.04	0.19	0.03			
		Night Wakings	0.01	0.24	0.00			
		Parasomnia	***0.27***	***0.11***	***0.25****			
		Sleep Disordered Breathing	0.16	0.22	0.07			
		Daytime Sleepiness	***0.34***	***0.10***	***0.39****			

***p*=<0.05, *** *p*=<0.001.**

2.8.2 Sleep as a predictor of Somatic Complaints

Sleep disturbances were associated with Somatic Complaints in the TD group, but not the clinical groups. Hierarchical multiple regression results examining the associations between Somatic Complaints and CSHQ variables are presented in Table 2.24. In the Autism group, composite sleep scores were not significant predictors of Somatic Complaints (ΔR^2 = 0.12, $\Delta F_{(1,55)}$ =0.94, p = 0.49), and neither were any subscales. In the FASD group, composite sleep scores were not significant predictors of Somatic Complaints (ΔR^2 = 0.04, $\Delta F_{(1,105)}$ =0.44, p = 0.89), and neither were any subscales. In the TD group however, composite sleep scores were significant predictors of Somatic Complaints (ΔR^2 = 0.36, $\Delta F_{(1,101)}$ =7.27, p = <0.001), as well as the subscales of Night Waking (**ß** = 0.18, p= 0.04), Sleep Duration SDB (**ß** = 0.41, p=<0.001) and Daytime Sleepiness (**ß** =0.31, p=0.003). After controlling for age, SES and sex, sleep disturbances explained 28% of the variance in Somatic Complaints in the Autism, and 7% in the FASD group (non-significant scores), but 44% in the TD group.

Group comparisons in Somatic Complaints

Raw Score: There were some significant differences and similarities between groups in the CBCL subscale of Somatic Complaints, with clinical groups scoring higher than the TD group. Overall, the tests of between subject effects on the Somatic Complaints subscale showed significant differences between the three groups ($F_{(2,\ 266)}$=13.26, p=<0.001, R^2=0.09). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=0.01; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher) but no significant similarities or differences between the FASD/ Autism groups. *Age*: There were significant age differences in the Autism and TD groups with older children scoring significantly higher than younger children (Autism: $F_{(21,56)}$=10.12, p=0.002, R^2=0.15; TD: ($F_{(1,103)}$=6.87, p=0.01, R^2=0.06) but not in the FASD group. Sex and SES were not significant predictors of Somatic Complaints in any of the groups.

Table 2.24: Hierarchical multiple regression results for CBCL subscale Somatic Complaints

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	-0.23	1.97		0.15	9.94	**0.15**
n= 68		Age	0.04	0.01	0.40			
		Sex	0.31	0.98	0.04			
		SES	-0.49	0.63	-0.10			
	2	(Constant)	-2.94	3.18		0.12	0.94	0.28
		Age	0.04	0.02	0.33			
		Sex	0.35	1.06	0.05			
		SES	-0.37	0.73	-0.07			
		Bedtime Resistance	0.16	0.20	0.16			
		Sleep Onset Delay	0.15	0.66	0.04			
		Sleep Duration	0.03	0.30	0.01			
		Sleep Anxiety	0.04	0.22	0.03			
		Night Wakings	0.39	0.32	0.22			
		Parasomnia	0.04	0.14	0.05			
		Sleep Disordered Breathing	0.05	0.25	0.03			
		Daytime Sleepiness	0.25	0.13	0.29			
FASD	1	(Constant)	3.05	1.57		0.01	1.11	0.01
n= 102		Age	0.01	0.01	0.13			
		Sex	0.93	0.63	0.15			
		SES	-0.21	0.53	-0.04			
	2	(Constant)	2.58	2.91		0.04	0.44	0.07
		Age	0.01	0.01	0.15			
		Sex	0.96	0.66	0.15			
		SES	0.13	0.57	0.02			
		Bedtime Resistance	0.05	0.17	0.05			
		Sleep Onset Delay	0.28	0.56	0.06			
		Sleep Duration	0.01	0.21	0.01			
		Sleep Anxiety	0.20	0.17	0.18			
		Night Wakings	0.05	0.22	0.03			
		Parasomnia	0.09	0.11	0.10			
		Sleep Disordered Breathing	0.24	0.20	0.14			
		Daytime Sleepiness	0.00	0.12	0.00			
TD	1	(Constant)	0.75	1.61		0.06	6.81	0.06
n= 101		Age	0.02	0.01	0.25			
		Sex	-0.58	0.57	-0.10			
		SES	-0.39	0.49	-0.08			
	2	(Constant)	-4.36	1.94		0.36	7.27	**0.44***
		Age	0.01	0.01	0.07			
		Sex	-0.15	0.48	-0.03			
		SES	0.04	0.43	0.01			
		Bedtime Resistance	0.04	0.12	0.04			
		Sleep Onset Delay	0.05	0.37	0.01			
		Sleep Duration	0.03	0.18	0.02			
		Sleep Anxiety	0.25	0.16	0.20			
		Night Wakings	***0.42***	***0.20***	***0.18****			
		Parasomnia	0.02	0.09	0.02			
		Sleep Disordered Breathing	***0.84***	***0.19***	***0.41****			
		Daytime Sleepiness	***0.25***	***0.08***	***0.31****			

***p*=<0.05, ** *p*=<0.001.**

2.8.3 Sleep as a predictor of Anxious Symptoms

Sleep disturbances were associated with Anxious Symptoms in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Anxious Symptoms and CSHQ variables are presented in Table 2.25. In the Autism group, composite sleep scores were significant predictors of Anxious Symptoms (ΔR^2 = 0.16, $\Delta F_{(1,55)}$ =1.19, p = 0.03), as well as the subscale of Sleep Anxiety (**ß** =0.40, p=0.05). In the FASD group, composite sleep scores were significant predictors of Anxious Symptoms (ΔR^2 = 0.12, $\Delta F_{(1,105)}$ =1.66, p = 0.02), as well as the subscales of Sleep Anxiety (**ß** = 0.31, p= 0.05) and SDB (**ß** = 0.24, p= 0.03). In the TD group, composite sleep scores were significant predictors of Anxious Symptoms (ΔR^2 = 0.20, $\Delta F_{(1,101)}$ =3.28, p = <0.001), as well as the subscale of Daytime Sleepiness (**ß** =0.41, p=<0.001). Sleep disturbances explained 26% of the variance in Anxious Symptoms in the Autism group, 24% in the FASD group and 32% in the TD group after controlling for age, SES and sex.

Group comparisons in Anxious Symptoms

Raw Score: Overall, the tests of between subject effects on the Anxious Symptoms subscale showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=19.36, p=<0.001, R^2=0.13). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher) and significant similarities between the FASD/ Autism groups when using the range of acceptability of 10% (p=<0.05). *Age*: There were no significant overall age differences in the Autism or FASD groups, but in the TD group age was significantly associated with Anxious Symptoms ($F_{(1,103)}$=10.72, p=0.001, R^2=0.10). Sex and SES were not significant predictors of Anxious Symptoms in any of the groups.

Table 2.25: Hierarchical multiple regression results for CBCL subscale Anxious

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1.00	(Constant)	7.75	3.69		0.07	4.13	**0.07***
n= 68		Age	0.05	0.03	0.27			
		Sex	1.33	1.83	0.10			
		SES	-1.45	1.19	-0.16			
	2.00	(Constant)	-2.64	5.85		0.16	1.19	**0.26***
		Age	0.05	0.03	0.26			
		Sex	2.20	1.95	0.16			
		SES	0.74	1.35	0.08			
		Bedtime Resistance	0.51	0.37	0.29			
		Sleep Onset Delay	1.35	1.21	0.18			
		Sleep Duration	0.02	0.56	0.01			
		Sleep Anxiety	***0.81***	***0.40***	***0.40****			
		Night Wakings	0.53	0.59	0.17			
		Parasomnia	0.10	0.25	0.06			
		Sleep Disordered Breathing	0.22	0.45	0.08			
		Daytime Sleepiness	0.34	0.23	0.22			
FASD	1.00	(Constant)	10.15	3.08		0.01	1.37	0.01
n= 102		Age	0.02	0.02	0.10			
		Sex	-1.20	1.23	-0.10			
		SES	0.26	1.03	0.02			
	2.00	(Constant)	1.85	5.45		0.12	1.66	**0.24***
		Age	0.03	0.02	0.14			
		Sex	-0.87	1.23	-0.07			
		SES	0.42	1.07	0.04			
		Bedtime Resistance	0.11	0.31	0.06			
		Sleep Onset Delay	1.14	1.04	0.13			
		Sleep Duration	0.33	0.38	0.10			
		Sleep Anxiety	***0.65***	***0.33***	***0.31****			
		Night Wakings	0.41	0.41	0.12			
		Parasomnia	0.35	0.21	0.22			
		Sleep Disordered Breathing	***0.81***	***0.37***	***0.24****			
		Daytime Sleepiness	0.14	0.22	0.07			
TD	1.00	(Constant)	1.18	3.78		0.10	10.61	**0.10**
n= 101		Age	0.07	0.02	0.32			
		Sex	-2.01	1.33	-0.15			
		SES	-0.66	1.14	-0.06			
	2.00	(Constant)	-12.87	5.14		0.20	3.28	**0.32***
		Age	0.04	0.02	0.16			
		Sex	-0.85	1.26	-0.06			
		SES	0.87	1.14	0.08			
		Bedtime Resistance	0.14	0.31	0.06			
		Sleep Onset Delay	1.07	0.99	-0.12			
		Sleep Duration	0.39	0.47	0.09			
		Sleep Anxiety	0.10	0.41	0.03			
		Night Wakings	0.52	0.54	0.09			
		Parasomnia	0.36	0.23	0.15			
		Sleep Disordered Breathing	0.23	0.49	0.05			
		Daytime Sleepiness	***0.79***	***0.21***	***0.41****			

***p*=<0.05, ** *p*=<0.001.**

2.8.4 Sleep as a predictor of Social Problems

Sleep disturbances were associated with Social Problems in the TD and FASD groups, but not the Autism group. Hierarchical multiple regression results examining the associations between Social Problems and CSHQ variables are presented in Table 2.26. In the Autism group, composite sleep scores were not significant predictors of Social Problems (ΔR^2 = 0.14, $\Delta F_{(1,55)}$ =0.89, p = 0.53), however there was a significant regression between Sleep Duration and Social Problems (**ß** = 0.30, p=0.05). In the FASD group, composite sleep scores were significant predictors of Social Problems (ΔR^2 = 0.23, $\Delta F_{(1,105)}$ =3.54, p = <0.001), as well as the subscales of Sleep Anxiety (**ß** = 0.30, p= 0.05) and Parasomnia (**ß** = 0.27, p= 0.03). In the TD group, composite sleep scores were significant predictors of Social Problems (ΔR^2 = 0.25, $\Delta F_{(1,101)}$ =3.77, p = <0.001), as well as the subscales of Parasomnia (**ß** = 0.21, p= 0.05) and Daytime Sleepiness (**ß** =0.32, p=0.01). Sleep disturbances explained 14% (non-significant score) of the variance in Social Problems in the Autism group, 24% in the FASD group and 27% in the TD group after controlling for age, SES and sex.

Group comparisons in Social Problems

Raw Score: Overall, the tests of between subject effects on the Social Problems subscale showed significant differences between the three groups with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=89.31, p=<0.001, R^2=0.40). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher), TD/FASD (p=<0.001; FASD group scoring higher) and FASD/ Autism groups (p=0.003; FASD group scoring higher). *Sex*: There were significant differences between boys and girls in the FASD group with girls scoring higher than boys (Fem: m=7.81 SD=2.89; Male: m=7.02, SD=3.42 conditions t(105)=0.96 p=0.04) but not in the Autism or TD groups. Age and SES were not predictors of Social Problems in any of the groups.

Table 2.26: Hierarchical multiple regression results for CBCL subscale Social Problems

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1.00	(Constant)	5.80	1.86		0.00	0.14	0.00
n= 68		Age	0.01	0.01	0.05			
		Sex	-0.15	0.92	-0.02			
		SES	-0.16	0.60	-0.04			
	2.00	(Constant)	1.49	3.01		0.14	0.89	0.14
		Age	0.00	0.01	0.05			
		Sex	0.10	1.01	0.02			
		SES	-0.04	0.70	-0.01			
		Bedtime Resistance	0.00	0.19	0.00			
		Sleep Onset Delay	0.13	0.62	0.04			
		Sleep Duration	***0.49***	***0.29***	***0.30****			
		Sleep Anxiety	0.04	0.21	0.04			
		Night Wakings	0.10	0.30	0.07			
		Parasomnia	0.10	0.13	0.13			
		Sleep Disordered Breathing	0.00	0.23	0.00			
		Daytime Sleepiness	0.01	0.12	0.01			
FASD	1.00	(Constant)	7.64	1.56		0.01	0.51	0.01
n= 102		Age	0.01	0.01	0.06			
		Sex	-0.53	0.62	-0.08			
		SES	-0.25	0.52	-0.05			
	2.00	(Constant)	1.36	2.59		0.23	3.54	**0.24****
		Age	0.01	0.01	0.07			
		Sex	-0.40	0.58	-0.06			
		SES	0.10	0.51	0.02			
		Bedtime Resistance	0.15	0.15	0.16			
		Sleep Onset Delay	0.46	0.50	0.11			
		Sleep Duration	0.30	0.18	0.18			
		Sleep Anxiety	***0.31***	***0.16***	***0.30****			
		Night Wakings	0.02	0.20	0.01			
		Parasomnia	***0.22***	***0.10***	***0.27****			
		Sleep Disordered Breathing	0.02	0.18	0.01			
		Daytime Sleepiness	0.09	0.11	0.09			
TD	1.00	(Constant)	3.31	1.36		0.00	0.01	0.00
n= 101		Age	0.00	0.01	0.01			
		Sex	-0.60	0.48	-0.13			
		SES	-0.32	0.41	-0.08			
	2.00	(Constant)	-2.27	1.82		0.25	3.77	**0.27****
		Age	-0.01	0.01	-0.14			
		Sex	-0.13	0.45	-0.03			
		SES	0.15	0.40	0.04			
		Bedtime Resistance	0.08	0.11	0.11			
		Sleep Onset Delay	0.36	0.35	0.12			
		Sleep Duration	0.32	0.17	0.21			
		Sleep Anxiety	0.12	0.15	0.12			
		Night Wakings	0.14	0.19	0.07			
		Parasomnia	***0.17***	***0.08***	***0.21****			
		Sleep Disordered Breathing	0.12	0.18	0.07			
		Daytime Sleepiness	***0.21***	***0.08***	***0.32****			

***p=<0.05, ** p=<0.001.**

2.8.5 Sleep as a predictor of Thought Problems

Sleep disturbances were associated with Thought Problems in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between Thought Problems and CSHQ variables are presented in Table 2.27. In the Autism group, composite sleep scores were significant predictors of Thought Problems (ΔR^2 = 0.32, $\Delta F_{(1,55)}$ =2.65, p = 0.02), as well as the subscale of Sleep Parasomnia (**ß** = 0.42, p=0.01). In the FASD group, composite sleep scores were significant predictors of Thought Problems (ΔR^2 = 0.22, $\Delta F_{(1,105)}$ =3.44, p = <0.001), as well as the subscales of Sleep Duration (**ß** = 0.30, p= 0.01) and Parasomnia (**ß** = 0.34, p= 0.01). In the TD group, composite sleep scores were significant predictors of Thought Problems (ΔR^2 = 0.35, $\Delta F_{(1,101)}$ =7.09, p = <0.001), as well as the subscales of SDB (**ß** = 0.36, p= <0.001), and Daytime Sleepiness (**ß** =0.30, p=0.01). Sleep disturbances explained 32% of the variance in Thought Problems in the Autism group, 24% in the FASD group and 45% in the TD group after controlling for age, SES and sex.

Group comparisons in Thought Problems

Raw Score: Overall, the tests of between subject effects on the Thought Problems subscale showed significant differences between the three groups, with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=48.27, p=<0.001, R^2=0.27). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group scoring higher) but no significant similarities or differences between the FASD/ Autism groups. Age, sex and SES were not significant predictors of Thought Problems in any of the groups.

Table 2.27: Hierarchical multiple regression results for CBCL subscale Thought Problems

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1	(Constant)	5.32	1.88		0.00	0.05	0.00
n= 68		Age	0.00	0.01	-0.03			
		Sex	0.23	0.93	0.04			
		SES	-0.24	0.60	-0.06			
	2	(Constant)	0.68	2.70		0.32	2.65	**0.32***
		Age	-0.01	0.01	-0.14			
		Sex	-0.02	0.90	0.00			
		SES	0.25	0.62	0.06			
		Bedtime Resistance	0.16	0.17	0.19			
		Sleep Onset Delay	0.24	0.56	0.07			
		Sleep Duration	0.16	0.26	0.10			
		Sleep Anxiety	0.04	0.19	0.04			
		Night Wakings	0.19	0.27	0.13			
		Parasomnia	***0.33***	***0.12***	***0.42****			
		Sleep Disordered Breathing	0.35	0.21	0.25			
		Daytime Sleepiness	0.14	0.11	0.18			
FASD	1	(Constant)	3.33	1.40		0.01	1.17	0.01
n= 102		Age	0.01	0.01	0.10			
		Sex	-0.07	0.56	-0.01			
		SES	0.35	0.47	0.07			
	2	(Constant)	-0.48	2.33		0.22	3.44	**0.24****
		Age	0.00	0.01	0.05			
		Sex	-0.01	0.53	0.00			
		SES	0.49	0.46	0.10			
		Bedtime Resistance	0.23	0.13	0.28			
		Sleep Onset Delay	0.24	0.45	0.06			
		Sleep Duration	***0.44***	***0.16***	***0.30****			
		Sleep Anxiety	0.17	0.14	0.18			
		Night Wakings	0.12	0.18	0.08			
		Parasomnia	***0.25***	***0.09***	***0.34****			
		Sleep Disordered Breathing	0.13	0.16	0.08			
		Daytime Sleepiness	0.09	0.10	0.10			
TD	1	(Constant)	2.53	1.18		0.029	3	0.029
n= 101		Age	0.01	0.01	0.14			
		Sex	-0.67	0.42	-0.16			
		SES	-0.83	0.36	-0.23			
	2	(Constant)	-3.53	1.43		0.35	7.09	**0.45****
		Age	0.00	0.01	0.03			
		Sex	0.29	0.35	0.07			
		SES	0.29	0.32	0.08			
		Bedtime Resistance	0.05	0.09	0.07			
		Sleep Onset Delay	0.13	0.27	0.05			
		Sleep Duration	0.02	0.13	0.02			
		Sleep Anxiety	0.21	0.11	0.22			
		Night Wakings	0.08	0.15	0.05			
		Parasomnia	0.06	0.07	0.08			
		Sleep Disordered Breathing	***0.55***	***0.14***	***0.36****			
		Daytime Sleepiness	***0.18***	***0.06***	***0.30****			

***p*=<0.05, ** *p*=<0.001.**

2.8.6 Sleep as a predictor of Attention Problems

Sleep disturbances were associated with Attention Problems in the FASD and TD groups, but not the Autism group. Hierarchical multiple regression results examining the associations between Attention Problems and CSHQ variables are presented in Table 2.28. In the Autism group, composite sleep scores were not significant predictors of Attention Problems (ΔR^2 = 0.18, $\Delta F_{(1,55)}$ =1.21, p = 0.32). In the FASD group, composite sleep scores were significant predictors of Attention Problems (ΔR^2 = 0.28, $\Delta F_{(1,105)}$ =4.71, p = <0.001), as well as the subscales of Bedtime Resistance (**ß** =0.44, p=0.01), Sleep Onset Delay (**ß** =0.25, p=0.03) and Parasomnia (**ß** =0.31, p=0.01). In the TD group, composite sleep scores were significant predictors of Attention Problems (ΔR^2 = 0.20, $\Delta F_{(1,101)}$ =3.56, p = <0.001), as well as the subscales of Night Wakings (**ß** =0.19, p= 0.05) and Daytime Sleepiness (**ß** =0.23, p=0.03). Sleep disturbances explained 18% (non-significant score) of the variance in Attention Problems in the Autism group, 29% in the FASD group and 36% in the TD group after controlling for age, SES and sex.

Group comparisons in Attention Problems

Raw Score: Overall, the tests of between subject effects on the Attention Problems subscale showed significant differences between the three groups, with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=111.61, p=<0.001, R^2=0.46). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) and TD/FASD groups (p=<0.001; FASD group soring higher) and FASD/ Autism groups (p=<0.001; FASD group scoring higher). *Sex*: There were no significant differences between the TD or Autism groups, but in the FASD group, girls scored significantly higher than boys (Fem: m=12.99 SD=3.94; Male: m=12.04, SD=4.48 conditions t(105)=1.01 p=0.02). SES and age were not significant predictors of Attention problems in any of the groups.

Table 2.28: Hierarchical multiple regression results for CBCL Subscale Attention Problems

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1.00	(Constant)	9.75	2.73		0.00	0.00	0.00
n= 68		Age	0.00	0.02	-0.01			
		Sex	0.29	1.35	0.03			
		SES	0.44	0.88	0.07			
	2.00	(Constant)	1.76	4.32		0.18	1.21	0.18
		Age	-0.01	0.02	-0.10			
		Sex	0.24	1.44	0.03			
		SES	1.40	1.00	0.22			
		Bedtime Resistance	0.13	0.27	0.11			
		Sleep Onset Delay	0.06	0.90	0.01			
		Sleep Duration	0.52	0.41	0.21			
		Sleep Anxiety	0.17	0.30	0.12			
		Night Wakings	0.47	0.43	0.21			
		Parasomnia	0.28	0.18	0.25			
		Sleep Disordered Breathing	0.12	0.33	0.06			
		Daytime Sleepiness	0.30	0.17	0.27			
FASD	1.00	(Constant)	12.39	1.97		0.00	0.04	0.00
n= 102		Age	0.00	0.01	0.00			
		Sex	-0.78	0.79	-0.10			
		SES	0.30	0.66	0.04			
	2.00	(Constant)	5.19	3.14		0.28	4.71	**0.29****
		Age	-0.01	0.01	-0.04			
		Sex	-0.42	0.71	-0.05			
		SES	0.72	0.62	0.11			
		Bedtime Resistance	***0.51***	***0.18***	***0.44****			
		Sleep Onset Delay	***1.37***	***0.60***	***0.25****			
		Sleep Duration	0.36	0.22	0.18			
		Sleep Anxiety	0.41	0.19	0.31			
		Night Wakings	0.07	0.24	0.03			
		Parasomnia	***0.33***	***0.12***	***0.31****			
		Sleep Disordered Breathing	0.30	0.22	0.14			
		Daytime Sleepiness	0.14	0.13	0.11			
TD	1.00	(Constant)	6.50	2.06		0.01	1.03	0.01
n= 101		Age	0.01	0.01	0.12			
		Sex	-2.82	0.73	-0.37			
		SES	-1.11	0.62	-0.17			
	2.00	(Constant)	-1.35	2.78		0.20	3.56	**0.36***
		Age	0.00	0.01	0.00			
		Sex	-2.25	0.68	-0.29			
		SES	-0.56	0.62	-0.09			
		Bedtime Resistance	0.14	0.17	0.11			
		Sleep Onset Delay	0.73	0.53	0.15			
		Sleep Duration	0.46	0.25	0.19			
		Sleep Anxiety	0.12	0.22	0.07			
		Night Wakings	***0.59***	***0.29***	***0.19****			
		Parasomnia	0.14	0.13	0.11			
		Sleep Disordered Breathing	0.36	0.27	0.13			
		Daytime Sleepiness	***0.25***	***0.11***	***0.23****			

***p=<0.05, ** p=<0.001.**

2.8.7 Sleep as a predictor of Delinquency

Sleep disturbances were associated with Delinquency in the Autism and TD groups. Hierarchical multiple regression results examining the associations between Delinquency and CSHQ variables are presented in Table 2.29. In the Autism group, composite sleep scores were significant predictors of Delinquency (ΔR^2 = 0.26, $\Delta F_{(1,55)}$ =2.27, p = 0.35), as well as the subscale of Sleep Anxiety (**ß** =0.37, p=0.05) and Daytime Sleepiness (**ß** = 0.42, p=<0.001). In the FASD group, composite sleep scores were not significant predictors of Delinquency (ΔR^2 = 0.05, $\Delta F_{(1,105)}$ =0.67, p =0.72). In the TD group, composite sleep scores were significant predictors of Delinquency (ΔR^2 = 0.24, $\Delta F_{(1,101)}$ =4.30, p = <0.001), as well as the subscales of SDB (**ß** = 0.24, p= 0.01) and Daytime Sleepiness (**ß** =0.40, p=<0.001). Sleep disturbances explained 35% of the variance in Delinquency in the Autism group, 9% (non-significant score) in the FASD group and 36% in the TD group after controlling for age, SES and sex.

Group comparisons in Delinquency

Raw Score: Overall, the tests of between subject effects on the Delinquency subscale showed significant differences between the three groups, with the FASD group scoring higher than the TD and Autism groups ($F_{(2, 266)}$=32.11, p=<0.001, R^2=0.20). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/FASD (p=<0.001; FASD group scoring higher) and FASD/Autism (<0.001; FASD group scoring higher) but no significant similarities or differences between the TD/Autism groups. *Age*: There were no significant overall age differences in the Autism, or TD groups but in the FASD group, delinquency was significantly associated with age ($F_{(1,105)}$=2.60, p=0.02, R^2=0.11). Sex and SES were not predictors of Delinquency in any of the groups.

Table 2.29: Hierarchical multiple regression results for Subscale Delinquency

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1.00	(Constant)	0.39	2.11		0.09	5.22	0.09
n= 68		Age	0.03	0.01	0.30			
		Sex	0.27	1.04	0.03			
		SES	-0.23	0.68	-0.05			
	2.00	(Constant)	-0.60	3.10		0.26	2.27	**0.35***
		Age	0.03	0.01	0.25			
		Sex	-0.14	1.04	-0.02			
		SES	-0.31	0.72	-0.06			
		Bedtime Resistance	0.24	0.20	0.24			
		Sleep Onset Delay	0.83	0.64	0.20			
		Sleep Duration	0.35	0.30	0.18			
		Sleep Anxiety	***0.43***	***0.21***	***0.37****			
		Night Wakings	0.13	0.31	0.07			
		Parasomnia	0.16	0.13	0.18			
		Sleep Disordered Breathing	0.12	0.24	0.07			
		Daytime Sleepiness	***0.38***	***0.12***	***0.42****			
FASD	1.00	(Constant)	2.93	2.18		0.02	2.60	0.02
n= 102		Age	0.02	0.01	0.16			
		Sex	0.18	0.87	0.02			
		SES	0.84	0.73	0.11			
	2.00	(Constant)	0.65	4.01		0.05	0.67	0.09
		Age	0.02	0.01	0.14			
		Sex	0.19	0.91	0.02			
		SES	0.54	0.79	0.07			
		Bedtime Resistance	0.07	0.23	0.05			
		Sleep Onset Delay	0.12	0.77	0.02			
		Sleep Duration	0.40	0.28	0.17			
		Sleep Anxiety	0.20	0.24	0.14			
		Night Wakings	0.04	0.30	0.02			
		Parasomnia	0.20	0.16	0.17			
		Sleep Disordered Breathing	0.16	0.28	0.07			
		Daytime Sleepiness	0.23	0.16	0.16			
TD	1.00	(Constant)	1.59	1.89		0.06	6.61	0.06
n= 101		Age	0.03	0.01	0.26			
		Sex	-1.55	0.67	-0.23			
		SES	-0.60	0.57	-0.10			
	2.00	(Constant)	-2.62	2.49		0.24	4.30	**0.36****
		Age	0.01	0.01	0.11			
		Sex	-1.17	0.61	-0.17			
		SES	0.12	0.55	0.02			
		Bedtime Resistance	0.05	0.15	0.05			
		Sleep Onset Delay	0.42	0.48	0.10			
		Sleep Duration	0.20	0.23	0.09			
		Sleep Anxiety	0.14	0.20	0.09			
		Night Wakings	0.30	0.26	0.11			
		Parasomnia	0.04	0.11	0.03			
		Sleep Disordered Breathing	***0.59***	***0.24***	***0.24****			
		Daytime Sleepiness	***0.39***	***0.10***	***0.40****			

***p=<0.05, ** p=<0.001.**

2.8.8 Sleep as a predictor of Aggression

Sleep disturbances were associated with higher levels of Aggression in the Autism, and TD groups. Hierarchical multiple regression results examining the associations between Aggression and CSHQ variables are presented in Table 2.30. In the Autism group, composite sleep scores were significant predictors of Aggression (ΔR^2 = 0.28, $\Delta F_{(1,55)}$ =2.29, p = 0.04), as well as the subscale of Daytime Sleepiness (**ß** = 0.36, p=0.01). In the FASD group, composite sleep scores were not significant predictors of Aggression (ΔR^2 = 0.09, $\Delta F_{(1,105)}$ =1.25, p = 0.28). In the TD group, composite sleep scores were significant predictors of Aggression (ΔR^2 = 0.27, $\Delta F_{(1,101)}$ =4.90, p =<0.001), as well as the subscale of Daytime Sleepiness (**ß** =0.37, p=<0.001). Sleep disturbances explained 30% of the variance in Aggression scores in the Autism group, 12% (non-significant score) in the FASD group and 38% in the TD group after controlling for age, SES and sex.

Group comparisons in Aggression

Raw Score: Overall, the tests of between subject effects on the Aggression subscale showed significant differences between the three groups, with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=49.13, p=<0.001, R^2=0.27). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher), TD/FASD (p=<0.001; FASD group scoring higher) and Autism/FASD groups (p=<0.001; FASD group scoring higher). *Age*: There were no significant overall age differences in the Autism, or FASD groups but in the TD group, age was significantly associated with Aggression scores ($F_{(1,103)}$=4.94, p=0.05, R^2=0.08). Sex and SES were not significant predictors of Aggression in any of the groups.

Table 2.30: Hierarchical multiple regression results for CBCL Subscale Aggression

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1.00	(Constant)	13.86	5.69		0.01	0.73	0.01
n= 68		Age	0.03	0.04	0.12			
		Sex	0.50	2.81	0.02			
		SES	-1.21	1.83	-0.09	0.28	2.29	**0.30***
	2.00	(Constant)	-3.14	8.36				
		Age	0.02	0.04	0.08			
		Sex	-0.79	2.79	-0.04			
		SES	-0.99	1.93	-0.07			
		Bedtime Resistance	0.56	0.53	0.22			
		Sleep Onset Delay	2.68	1.73	0.24			
		Sleep Duration	1.56	0.80	0.31			
		Sleep Anxiety	0.50	0.58	0.17			
		Night Wakings	0.11	0.84	0.02			
		Parasomnia	0.20	0.36	0.09			
		Sleep Disordered Breathing	0.24	0.64	0.06			
		Daytime Sleepiness	***0.84***	***0.33***	***0.36****			
FASD	1.00	(Constant)	27.42	4.49		0.02	2.11	0.02
n= 102		Age	-0.04	0.03	-0.16			
		Sex	-1.87	1.79	-0.10			
		SES	0.67	1.51	0.04			
	2.00	(Constant)	16.22	8.08		0.09	1.25	0.12
		Age	-0.04	0.03	-0.16			
		Sex	-1.84	1.83	-0.10			
		SES	1.05	1.59	0.07			
		Bedtime Resistance	0.26	0.46	0.10			
		Sleep Onset Delay	0.86	1.55	0.07			
		Sleep Duration	0.89	0.57	0.19			
		Sleep Anxiety	0.48	0.48	0.16			
		Night Wakings	0.51	0.61	0.10			
		Parasomnia	0.44	0.32	0.18			
		Sleep Disordered Breathing	0.51	0.55	0.10			
		Daytime Sleepiness	0.13	0.33	0.05			
TD	1.00	(Constant)	9.08	5.04		0.05	4.89	0.05
n= 101		Age	0.06	0.03	0.22			
		Sex	-4.27	1.78	-0.23			
		SES	-2.06	1.53	-0.13			
	2.00	(Constant)	-12.00	6.52		0.27	4.90	**0.38***
		Age	0.02	0.03	0.06			
		Sex	2.59	1.60	0.14			
		SES	0.10	1.45	0.01			
		Bedtime Resistance	0.39	0.39	0.13			
		Sleep Onset Delay	1.81	1.25	0.16			
		Sleep Duration	0.66	0.59	0.11			
		Sleep Anxiety	0.25	0.52	0.06			
		Night Wakings	1.19	0.68	0.16			
		Parasomnia	0.43	0.30	0.14			
		Sleep Disordered Breathing	1.14	0.63	0.18			
		Daytime Sleepiness	***0.94***	***0.27***	***0.37****			

***p=<0.05, ** p=<0.001.**

2.8.9 Sleep as a predictor of Behaviour

Sleep disturbances were associated with CBCL Total Score in the Autism, TD and FASD groups. Hierarchical multiple regression results examining the associations between CBCL Total Score and CSHQ variables are presented in Table 2.31. In the Autism group, composite sleep scores were significant predictors of CBCL Total Score (ΔR^2 = 0.25, $\Delta F_{(1,55)}$ =2.04, p = 0.05), as well as the subscale of Sleep Duration (**ß** =0.27, p=0.04) and Daytime Sleepiness (**ß** = 0.41, p=0.01). In the FASD group, composite sleep scores were significant predictors of CBCL Total Score (ΔR^2 = 0.13, $\Delta F_{(1,105)}$ =1.86, p = 0.04), as well as the subscales of Sleep Duration (**ß** = 0.23, p= 0.04) and Sleep Anxiety (**ß** = 0.27, p= 0.04). In the TD group, composite sleep scores were significant predictors of CBCL Total Score (ΔR^2 = 0.30, $\Delta F_{(1,101)}$ =5.95, p = <0.001), as well as the subscales of SDB (**ß** = 0.20, p= 0.04) and Daytime Sleepiness (**ß** =0.42, p=<0.001). Sleep disturbances explained 33% of the variance in Total CBCL scores in the Autism group, 25% in the FASD group and 43% in the TD group after controlling for age, SES and sex.

Group comparisons in CBCL Total Score

Raw Score: Overall, the tests of between subject effects on the CBCL Total Score subscale showed significant differences between the three groups, with clinical groups scoring higher than the TD group ($F_{(2, 266)}$=71.02, p=<0.001, R^2=0.35). In post-hoc analysis and tests of similarity, there were significant differences in raw scores between the TD/ Autism (p=<0.001; Autism group scoring higher) TD/FASD (p=<0.001; FASD group scoring higher) and FASD/ Autism groups (p=<0.001; FASD group scoring higher). *Age*: There were no significant overall age differences in the FASD group, but in the Autism and TD groups, age was significantly associated with total CBCL scores (Autism: $F_{(1,56)}$=4.13, p=0.05, R^2=0.07; TD $F_{(1,103)}$=7.45, p=0.01, R^2=0.07). Sex and SES were not significant predictors of CBCL Total Scores in any of the groups.

Table 2.31: Hierarchical multiple regression results for CBCL Total

			Overall Model			Change Statistics		
Group	**Block**	**Predictors**	***B***	***SE B***	**ß**	**ΔR^2**	**ΔF^2**	**R^2**
Autism	1.00	(Constant)	44.01	14.51		0.07	4.06	0.07
n= 68		Age	0.20	0.10	0.27			
		Sex	3.48	7.18	0.06			
		SES	-3.36	4.66	-0.10			
	2.00	(Constant)	-10.04	21.67		0.25	2.04	**0.33***
		Age	0.14	0.10	0.19			
		Sex	2.76	7.24	0.05			
		SES	-0.04	5.00	0.00			
		Bedtime Resistance	0.32	1.36	0.05			
		Sleep Onset Delay	1.68	4.49	0.06			
		Sleep Duration	***3.58***	***2.07***	***0.27****			
		Sleep Anxiety	0.16	1.49	0.02			
		Night Wakings	0.39	2.17	0.03			
		Parasomnia	0.63	0.92	0.10			
		Sleep Disordered Breathing	0.52	1.67	0.05			
		Daytime Sleepiness	***2.47***	***0.85***	***0.41****			
FASD	1.00	(Constant)	69.02	12.81		0.01	0.70	0.01
n= 102		Age	0.06	0.08	0.07			
		Sex	-3.15	5.11	-0.06			
		SES	2.03	4.30	0.05			
	2.00	(Constant)	24.89	22.52		0.13	1.86	**0.25***
		Age	0.05	0.08	0.07			
		Sex	-2.05	5.09	-0.04			
		SES	3.38	4.43	0.08			
		Bedtime Resistance	1.43	1.29	0.19			
		Sleep Onset Delay	4.51	4.31	0.12			
		Sleep Duration	***3.08***	***1.58***	***0.23****			
		Sleep Anxiety	***2.30***	***1.35***	***0.27****			
		Night Wakings	1.43	1.71	0.10			
		Parasomnia	0.64	0.88	0.09			
		Sleep Disordered Breathing	1.43	1.54	0.10			
		Daytime Sleepiness	0.25	0.92	0.03			
TD	1.00	(Constant)	25.89	15.58		0.07	7.38	0.07
n= 101		Age	0.24	0.09	0.26			
		Sex	-13.18	5.49	-0.23			
		SES	-6.54	4.72	-0.14			
	2.00	(Constant)	-44.10	19.50		0.30	5.95	**0.43****
		Age	0.08	0.08	0.09			
		Sex	7.54	4.78	0.13			
		SES	0.30	4.32	0.01			
		Bedtime Resistance	0.99	1.17	0.10			
		Sleep Onset Delay	4.67	3.74	0.13			
		Sleep Duration	1.65	1.77	0.09			
		Sleep Anxiety	0.46	1.56	0.04			
		Night Wakings	3.24	2.03	0.14			
		Parasomnia	1.41	0.89	0.14			
		Sleep Disordered Breathing	***3.99***	***1.87***	***0.20****			
		Daytime Sleepiness	***3.34***	***0.80***	***0.42****			

***p=<0.05, ** p=<0.001.**

2.8.10 CBCL Summary

Children with FASD and Autism scored consistently higher than the TD group in every CBCL subscale. Children in the FASD group tended to score higher than children with FASD. Syndrome specificity (occasions where there were significant differences between all three groups) were noted in the subscale of Delinquency. Children with FASD and Autism had significantly similar Withdrawn scores.

Developmental changes were apparent in the three groups. Age was a significant predictor of Withdrawn and Delinquency symptoms in the FASD group, with older children scoring higher than younger children. Children with Autism scored higher in the Withdrawn, Somatic and Total categories with increasing chronological age. In the TD group, age was a significant predictor of Withdrawn, Somatic, Anxious, Aggression and Total CBCL scores.

There were some sex related differences. Girls with FASD scored significantly higher than boys in Attention and Social problems.

Behaviour scores were significantly associated with sleep problems in all three groups In the Autism group, Sleep Anxiety, Daytime Sleepiness and Parasomnias accounted for the largest amount of variance in behavioural problems; in total, 33% of the variance in CBCL scores were attributable to sleep problems. In the FASD group, Sleep Duration, Sleep Anxiety and Parasomnias accounted for the largest amount of variance in behavioural problems; in total, 25% of the variance in CBCL scores were attributable to sleep problems. In the TD group, Daytime Sleepiness, Parasomnias and SDB accounted for the largest amount of variance in behavioural problems; in total, 43% of the variance in CBCL scores were attributable to sleep problems.

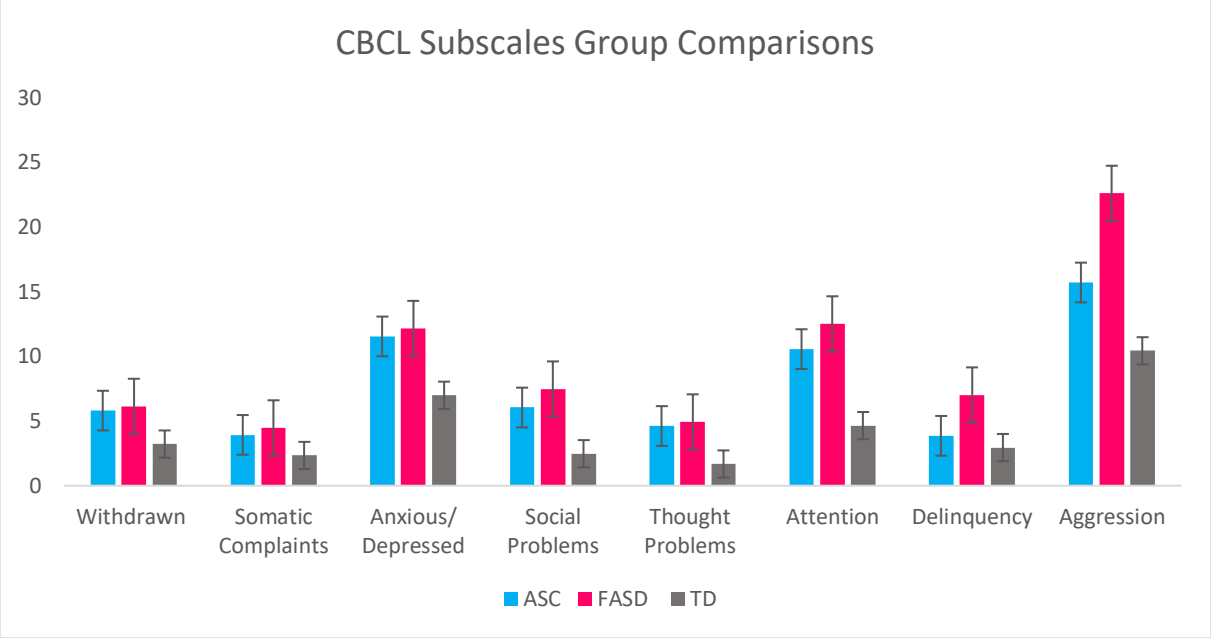


Figure 2.7: Comparison between Autism, FASD and TD scores on the CBCL subscales (SE bars)

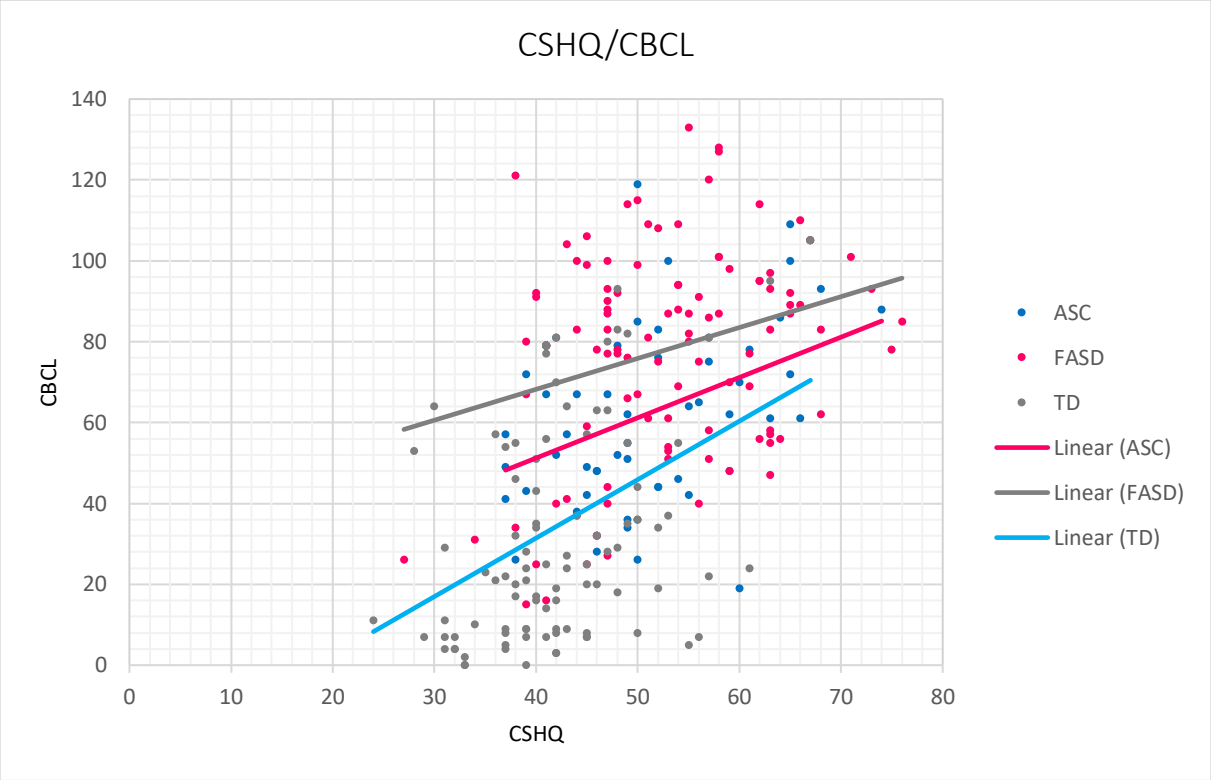


Figure 2.41: Scatter plot showing raw scores: sleep (CSHQ) against behaviour (CBCL)

2.9 Discussion

This study aimed to assess sleep, anxiety, behaviour and executive functioning in the three samples, using a sample large enough to test whether these domains are syndrome specific, and whether inferences can be made about their relationship with sleep variables. In meeting these aims this study was successful; the CSHQ, SCAS, BRIEF and CBCL were administered to 277 caregivers and statistical analysis revealed an interesting set of similarities, differences and relationships both within and between groups. Some of these results have implications for the social, emotional and behavioural care and education of children with Autism and FASD. Results that appeared to be domain specific and significantly associated with sleep are set out in the following section, together with a discussion of where these results sit within current literature.

2.9.1 Supported, partially supported and non-supported hypotheses.

1) a) Children with FASD and Autism will present with higher scores in the BRIEF, SCAS and CBCL than TD children. (Kodituwakku, 2009, Lange 2017). This hypothesis was partially supported by the results. According to parental report, children with Autism and FASD scored significantly higher than their TD peers on most subscales, but not all. There were minimal differences between the clinical and TD groups on the SCAS subscale of physical injury, and there were no differences between the Autism and TD group on the subscale of social phobia. There were no significant differences between the Autism and TD group on the CBCL subscale of Delinquency. There were also syndrome specific, proportional, mean scores. These can be seen in figures 2.6-2.8 and are discussed further.

2) a) Children with FASD will present with a higher number of attentional and conduct problems than TD or children with Autism (Popova, Lange, Shield, et al., 2016). This hypothesis was supported by the results. According to parental report, there were no significant differences between the Autism and TD group on the CBCL subscale of Delinquency, whilst children with FASD scored significantly higher in the subscales of attention and delinquency than their peers.

b) Children with Autism will present with a higher number of social and communication difficulties than children with FASD (Stevens et al., 2013). This hypothesis was not supported by the results. It was predicted that children with Autism would present with higher numbers of social and communication difficulties than children with FASD, however children with FASD scored consistently higher in externalising and social problems than their peers.

c) Children with FASD and Autism will present with a higher number of sleep problems than TD children (Inkelis & Thomas, 2018; Mazzone et al., 2018). This hypothesis was partially supported by the results. According to parental report, children with FASD and Autism scored significantly higher than TD children in the subscales of sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnia, daytime sleepiness and total CSHQ, but not on SDB and bedtime resistance scores. Seventy two percent of the FASD sample scored above the clinical cut off point for sleep disorders on the CSHQ. Sixty one percent of the Autism sample and 41% of the TD sample scored above the point of clinical cut off. This high percentage of TD children scoring above the clinical cut off was unexpected.

3) Sleep habits will be significantly correlated with executive functioning, behaviour and anxiety in the three groups. (Cohen, Conduit, Lockley, Rajaratnam, & Cornish, 2014; Gregory & Sadeh, 2012; Wengel, Hanlon-Dearman, & Fjeldsted, 2011). This hypothesis was supported by the results. Several statistical associations were found in every subscale and the present data reveal that, according to caregiver report, there are associations between sleep, anxiety, executive functioning and behaviour in Autism, FASD and TD groups. Furthermore, there were syndrome specific statistical associations between sleep and psychological outcomes, which appear to cluster around certain sleep variables in certain populations (Figure 2.5).

4) a) There will be higher anxiety scores amongst girls than boys in all three groups. (Buckhalt et al., 2007; Kodituwakku, 2009); b) There will be higher maladaptive behaviour scores amongst boys than girls in all three groups (Buckhalt et al., 2007; Kodituwakku, 2009; Mukherjee, Wray, Commers, Hollins, & Curfs, 2013; Werling & Geschwind, 2013) This was partially supported. Across the three groups, sex was a significant predictor of separation anxiety, physical injury, social problems, working memory, shifting, planning and organising, organisation of materials, monitoring, inhibition, initiation and emotional control. In accordance with previous studies,

girls tended to score higher than boys on psychometric scores, however in the Autism group this was not the case. Whilst sex was a significant predictor in the Autism group on several subscales, it was not in line with previous studies in which girls tend to score higher than boys in psychometric scores – both boys and girls in the Autism group scored highly at different points.

c) Age will predict severity of sleep disturbances, maladaptive behaviour and anxiety in the three groups. (Buckhalt et al., 2007; Kodituwakku, 2009; Mukherjee, Wray, Commers, Hollins, & Curfs, 2013) This hypothesis was not supported by the results. Age was a significant predictor of several subscales across the three groups and scores did not necessarily improve with age in the TD group.

d) SES will be a predictor of sleep, behaviour and anxiety in the three groups (Buckhalt et al., 2007; Kodituwakku, 2009; Mukherjee, Wray, Commers, Hollins, & Curfs, 2013; Werling & Geschwind, 2013).This hypothesis was not supported by the results. Across the three groups socioeconomic status was a significant predictor of sleep onset delay, parasomnia, working memory, shifting and organising materials, with those from lower SES backgrounds tending to score higher on psychometric scores.

The findings here provide evidence that sleep problems are more prevalent in children with Autism and FASD than in TD children. The present results reveal that, according to caregiver report, sleep problems predict behaviour, executive functioning and anxiety in children with Autism and FASD. Furthermore, it appears that psychological outcomes cluster around certain sleep variables, according to syndrome. This can be viewed in Figure 2.8.

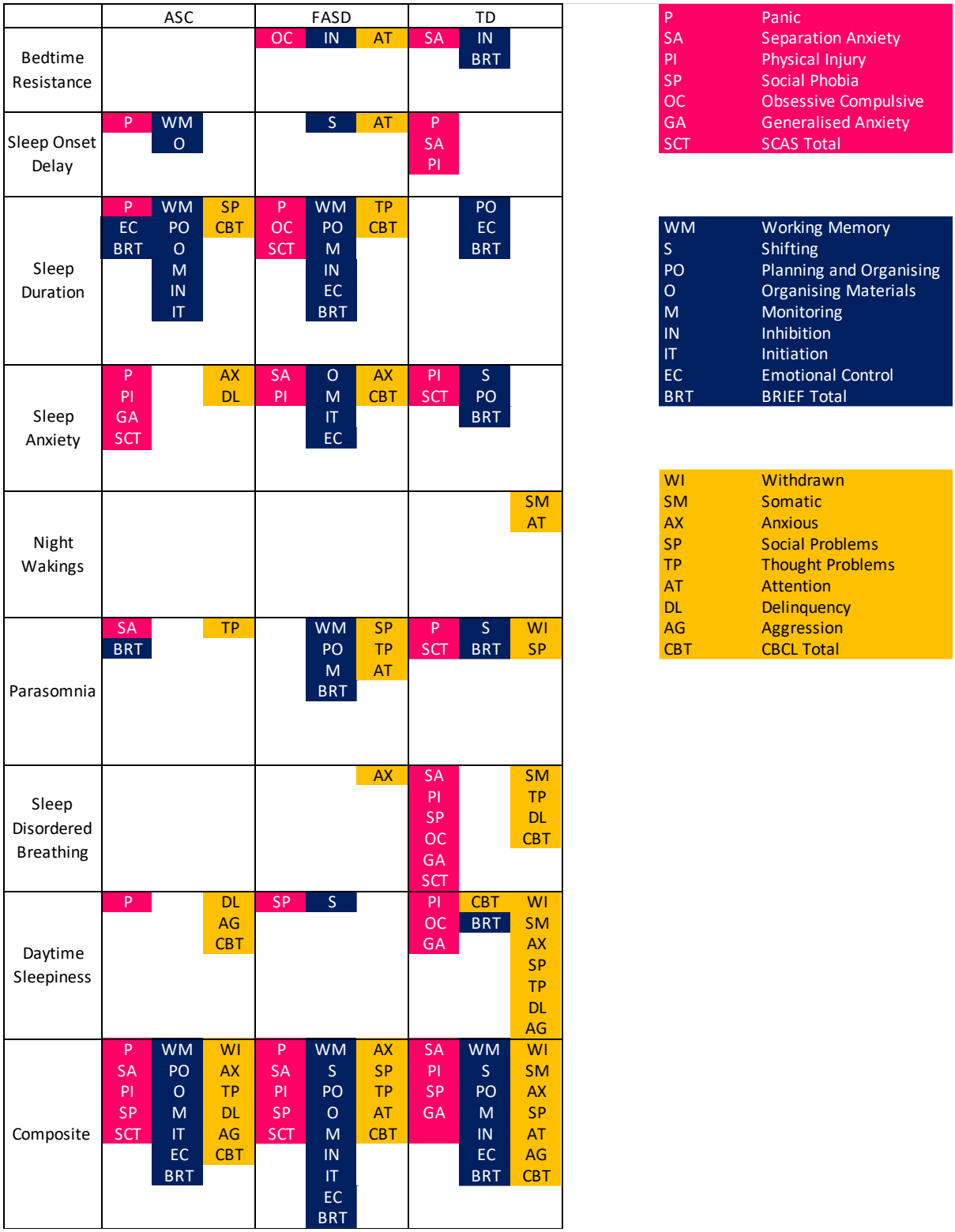


Figure 2.8: Significant regressions (p<0.05) between sleep variables and psychometric outcomes, ordered by syndrome. Significant regressions appear to cluster around different areas. For example, the top right box (TD/Bedtime Resistance) shows that SA (Separation Anxiety), IN (Inhibition) and BRT (BRIEF total) were significantly associated with Bedtime Resistance in the TD group.

2.9.2 The Children's Sleep Habits Questionnaire (CSHQ)

2.9.2.1 Bedtime Resistance

The present results reveal that bedtime resistance was significantly associated with obsessive compulsive, inhibition and attention related behaviour in the FASD sample. Bedtime resistance was significantly associated with separation anxiety, inhibition and composite executive functioning scores in the TD group, but not significantly associated with any subscales in the Autism group. The sleep behaviour of resisting and refusing the bedtime routine is common in younger children in TD populations who have yet to understand the concept of bedtime, learn to self sooth or be comfortable on their own. It can include noncompliant behaviours that make bedtime routines longer than necessary, such as refusing or stalling the bedtime routine, becoming distressed or making multiple 'curtain calls'. In populations where there is a discrepancy between mental age and chronological age (MA and CA), bedtime resistance can still present behaviourally with refusals, meltdowns or curtain calls, but with the added complexities that being an older child with a neurodevelopmental condition brings. The present results suggest that executive functioning domains are significantly correlated with bedtime resistant behaviours. Inhibition, for example, is measured on the BRIEF as the ability to resist impulses and stop one's own behaviour at the appropriate time. For a child presenting with clinical levels of inhibitory control/ impulsivity, who doesn't feel the need to go to bed, bedtime resistance may look like a desire to stay awake, keep playing or keep engaged in activities. For a child presenting with clinical levels of compulsion, similarly, bedtime resistance can present as a persistent, uncontrollable need to engage in activities other than bedtime, if the child has not 'bought into' the concept of bedtime or does not understand the need to engage in the process of the bedtime routine. Children with FASD who presented with impulsive, attentional and compulsive behaviour were more likely to resist bedtimes. However, this is not true of the TD or Autism group, which leads to the question of whether this particular cluster of behavioural characteristics is syndrome specific. Perhaps it is because, as is reported later in this discussion, children with FASD are much more likely than the

TD and Autism population to engage in delinquency and aggressive behaviours, and as a result have more of an ability and inclination to act on rule-breaking impulses which can manifest as bedtime resistance.

Unexpectedly, a high proportion of TD children also appeared to show bedtime resistance at similar levels to the clinical group and is probably why there is no significant difference between the clinical and TD groups on this subscale. This could be attributable to selection bias in this sample and is not consistent with previous CSHQ studies on FASD and children with Autism (Díaz-Román et al., 2018; Inkelis & Thomas, 2018).

2.9.2.2 Sleep Onset Delay

Sleep onset delay is measured on the CSHQ from one question: 'child falls asleep within 20 minutes after going to bed', based on the assumption that when the average sleep latency of a child is above 20-30 minutes it is classified as disruptive. Sleep onset delay was significantly higher in the clinical groups than the TD group, and significantly similar between FASD and Autism. A number of theoretical reasons may underline this, such as the inability to self-soothe (as with bedtime resistance), excessive rumination, or inability to relax. In populations where MA is lower than CA the learnt behaviour of self-soothing tends to be underdeveloped (Meltzer & Mindell, 2006) and it was expected therefore that children within the clinical groups would score higher in the category of sleep onset delay. Outcomes related to attention and executive control clustered around sleep onset delay in the two clinical groups: working memory, organisation of materials and panic were closely associated with sleep onset delay in the Autism group, whilst shifting and attention were associated with sleep onset delay in the FASD group. Meanwhile in the TD group, anxiety symptoms were more closely associated with sleep onset delay. Since this is the first study to analyse these variables in the FASD population, these associations would benefit from replications from further studies. Nonetheless sleep onset delay was a significant predictor of attention and working memory in the FASD group, which fits the

profile of the child who cannot self sooth at bedtime as a result of problems with executive or attentional control. Similarly, this is the first study to use the CSHQ with the BRIEF in the Autism population, however sleep and executive function have been examined previously using other instruments. Consistent with previous similar work, the present study found that sleep onset delay in the Autism sample was associated with executive functioning subscales. For example Tsung-Han Tsai and colleagues (2019) conducted a large scale study assessing 8-14 year olds (*n*=6832) for Autism traits and sleep deficits, finding that sleep was a significant moderator for Autism traits (measured by executive functioning parameters) in the general population, and that cognitive inflexibility or repetitive, obsessive or impulsive behaviour was a predictor of sleep onset delays (Tsai, Chen, & Gau, 2019).

2.9.2.3 Sleep Duration

Sleep duration is measured by the CSHQ as a composite of three questions: 'child sleeps the right amount'; 'child sleeps the same amount every day' and 'child sleeps too little'. Asking a parent is an obvious measure of whether a child is sleeping for long enough but is often estimated erroneously by caregivers, particularly those with older children for whom sleep latency or night waking might be less known (Meltzer & Mindell, 2006).

According to caregiver responses, sleep duration appeared to be significantly lower in the clinical groups than the TD group. Additionally, sleep duration predicted several anxiety, behaviour and executive functioning concerns. The present study found a considerable number of executive functioning domains clustered around sleep duration in the three groups. In the Autism group, sleep duration was a significant predictor of every BRIEF subscale apart from 'shifting', as well as BRIEF total. In the FASD group, sleep duration was a significant predictor of working memory, planning and organising, monitoring, inhibition, emotional control and BRIEF total. In the TD group, sleep duration was a significant predictor of shifting, planning and organising and BRIEF total. Given the large number

of BRIEF subscales that were significantly associated with the amount that children sleep, as well as evidence from previous studies in Autism and TD populations (Tsai et al., 2019; Wilckens, Woo, Kirk, Erickson, & Wheeler, 2014), and the strength of pre and post hoc power analyses, a claim can be made from the present data that there exists an association between executive functioning and sleep duration in children with FASD. With this in mind, a recommendation can be made here for the pressing need for sleep intervention studies in this population, to investigate whether adequate sleep may ameliorate executive functioning in the FASD population.

2.9.2.4 Sleep Anxiety

Sleep anxiety was the biggest predictor of anxiety and delinquency symptoms in the Autism group. This is consistent with previous findings examining SCAS and CSHQ in Autism, where anxiety was associated with sleep problems in a sample (*n*=167) of children aged between 5 and 18 years (Rzepecka et al., 2011). In the FASD sample, sleep anxiety was a predictor of clinical anxiety, separation anxiety, thought problems, behaviour composite, and a cluster of executive functioning subscales and BRIEF total. This, in particular the association with separation anxiety and thought problems, is likely due to the consistent engagement in negative rumination that is common in both children with FASD and Autism. Both clinical groups tend to 'live in imaginary worlds', however when additional negative experiences are present, the child is more likely to live in a *negative* imaginary world which can impact multiple areas of life.

The development of the imagination involves a critical period in which the child learns to explore and differentiate what is real and what is imaginary. Television characters, fictional creatures and fantasy may seem obviously imaginary to an adult but can be very real for young children. Early childhood anxieties tend to focus on imaginary, magical, supernatural or fictional creatures; during this time sleep anxiety can result from common childhood fantasy fears, for example of monsters, witches, the dark, etc (Mindell & Owens, 2015). Older children tend to have fears of realistic perceived threats,

such as school or social anxieties, performance anxieties, friendship problems or catastrophic news events (Mindell & Owens, 2015). To this extent, irrational fears and worries may also play a part in anxieties in older children, and for children who experience nightmares, going to bed can be a distressing and anxious time. Night-time anxieties can result in increased bedtime resistance and sleep onset delay, bedtime refusals or battles with caregivers, lying awake and ruminating, or distracting from worries by engaging in increased screen time (Hale & Guan, 2015). Additionally, when there is trauma in a child's early life, anxieties will and ruminations tend to be more intense and constantly present; therefore sleep anxiety amongst TD children with early life trauma and attachment issues, who have experienced multiple caregivers, tends to be higher than TD children with no trauma (Trejos-Castillo & Trevino-Schafer, 2018). This is significant in the present population of children with FASD, the majority of whom were in the care of a foster or adoptive parent or biological relative other than the biological parent. Children with Autism can tend to show high levels of creative imagination and visual imagery (Crespi, Leach, Dinsdale, Mokkonen, & Hurd, 2016; Scott, 2013) despite claims to the contrary (Craig, 2001). One striking similarity between children with FASD and Autism is that both tend to 'live in imaginary worlds' sometimes containing a rich array of vivid imagery and fantasy characters (Catterick & Curran, 2014; P. E. Davis, Simon, Meins, & Robins, 2018). Clinical and educational professionals note that children with FASD tend to display vivid imaginations and creative thinking (Catterick & Curran, 2014) but similar to children with Autism appear less able to do so when it comes to playing with others, or when prescribed imaginary things to think about (Bishop et al., 2007).

It was expected therefore that sleep anxiety amongst both the FASD and Autism groups would be higher than the TD group. According to caregiver responses, children with FASD and Autism experienced significantly higher levels of sleep anxiety than their TD peers. Additionally, Autism and FASD sleep anxiety scores were significantly similar. The present study found that sleep anxiety increased with CA in the FASD group and was significantly higher in girls than boys with Autism. This is consistent with previous findings in Autism, in which sleep anxiety was at higher levels than typical

controls. In one study conducted by Gunes and colleagues (2019) assessing sleep and Autism traits in a sample (*n*=112) of children and adolescents with Autism diagnoses aged between 2-18 years, sleep anxiety was significantly higher in their clinical sample than their TD sample (t(222)=2.48, *p*=0.01). The higher sleep anxiety levels in the clinical groups may be attributable to a number of factors. Firstly, children with Autism and FASD tend to experience higher levels of daytime anxiety which can transfer into night-time fears (Kambeitz et al., 2019; Keen, Adams, Simpson, den Houting, & Roberts, 2019). Secondly, both children with Autism and FASD present with atypical developments of imagination, mental imagery, deciphering real from fiction, and mental creativity (Scott, 2013). Children with FASD and Autism become 'lost' in thought which may have played a role in sleep anxiety and the delaying of bedtime.

2.9.2.5 Night Waking

There were no significant associations between night waking and anxiety, behaviour or executive functioning symptoms in the Autism or FASD groups. Night waking has previously been reported to correlate with Autism traits based around executive functioning factors. In the previously mentioned study by Gunes and colleagues (2019), night waking as measured on the CSHQ significantly correlated with Autism traits as measured by the Childhood Autism Rating Scale (CARS; R^2=0.04; *p*=0.05) but measured with effect size thresholds below the threshold for the present study. Of the two previous studies assessing CSHQ parameters in children with FASD, one (Wengel et al., 2011) calculated the correlation between CSHQ parameters and daytime functioning, finding that night waking was correlated with the Sensory Profile parameters of low endurance/ tone (Spearman Correlation [SC]=0.58, p=0.023), registration (SC=0.543, *p*=0.04), modulation of visual and emotional input affecting activity (SC=0.662, *p*=0.007) and emotional/social responses to sensory input (SC=0.610, *p*=0.016). It is unfortunate that regression (rather than correlational) data were not published here, which would shed more light on the similarities and discrepancies between the present results and those of Wengel and her colleagues. In the present study however, night waking was a significant

predictor of attentional problems and somatic complaints in the TD group. This concurs with a sleep restriction study conducted by Kahn and colleagues (2014) in healthy neurotypical adults (*n*=61), where night wakings were a significant predictor of attentional differences, including reduced reaction time and increased commission and omission errors.

The present results reveal that children in the two clinical groups experienced significantly more night wakings than TD children. Sleep cycles in primary school aged children last around 90 minutes, at the end of which there is usually a short arousal (see Section 1.1.2). Typically, children should be able to fall back asleep after waking after a sleep cycle. In preschool TD children, one of the most common complaints is multiple night wakings that require parental assistance to return back to sleep (Mindell & Owens, 2015). This is usually due to negative sleep onset associations, where the child associates their ability to fall asleep with certain conditions, environments, or caregivers present, such as being held, rocked or nursed, or having a story read prior to sleep time. Night-time waking is normal, even in adults, as the end of the sleep cycle will usually end in an arousal, after which an individual should be able to fall back asleep. However, if at the end of a sleep cycle the child has woken up and is expecting the same conditions as when he fell asleep (or was put to sleep), the night-time waking will tend to result in calling for parental assistance. If, additionally, the child has a sleep onset delay, sleep anxiety, bedtime resistance, or experiences nightmares, it can put further strain on the caregiver and delay the child further from going back to sleep after a night waking. Furthermore, atypical neurobiological functioning in both clinical groups may impact the sleep-wake process. In both Autism and FASD populations, atypical hypothalamic control of sleep and wakefulness (including SCN abnormalities) GABA maturation and melatonin secretion are thought to play a role in interfering with the sleep-wake process (Giannotti et al., 2002; Goril et al., 2012).

Night waking is amongst the most common complaints for caregivers of children with Autism and FASD (Jan et al., 2010). According to parental reports, night waking is common for periods of 2-3 hours in children with Autism during which time the child may be fully awake, laugh, talk, scream or get up

and play with toys or various objects in the room, while sleep onset and night waking problems are associated with poor sleep hygiene or maladaptive sleep associations (Cortesi, Giannotti, Ivanenko, & Johnson, 2010). Night wakings are prevalent in children with FASD, according to parental report (Chen et al., 2012), PSG (Chen et al., 2012; Goril et al., 2016) and actigraphy (Wengel, Hanlon-Dearman, & Fjeldsted, 2011b). The present findings are in agreement with these previous reports of night waking in Autism and FASD. According to caregiver report, children with Autism and FASD experienced significantly more night wakings than TD children.

2.9.2.6 Parasomnia

The CSHQ measures parasomnia through seven questions asking whether the child talks in their sleep, moves around during sleep, sleepwalks during the night, wets the bed at night, grinds teeth during sleep, is alarmed by a frightening dream, or awakens at night screaming, sweating, inconsolable. An additional question was added asking caregivers to describe the content of nightmares, the raw data is included in the Appendix section of this thesis. In the present study the most frequently mentioned problems amongst children with FASD in the CSHQ and CBCL were nightmares, usually centred around persecution, frightening creatures, family members being taken away or dying. Persecutory nightmares are common in children with early life trauma and in foster care (Trejos-Castillo & Trevino-Schafer, 2018), and can be triggered by changes in environment, further trauma, or being reminded of trauma (Meltzer & McLaughlin Crabtree, 2015).

Children in the clinical groups were significantly more likely to experience parasomnias than TD children, although one critique of using the CSHQ in clinical populations is that the parasomnia subscale incorporates enuresis – which might often explain the high score in syndromic children, but might also be associated with the developmental stage of the child rather than an underlying psychopathology. In the present study, parasomnia was a predictor of BRIEF total score, separation anxiety, and thought problems in the Autism group, whereas parasomnia was associated with SCAS

total score and symptoms of panic in the TD group. In the FASD group, several BRIEF subscales were significantly associated with parasomnia, but no anxiety scores. This seems to suggest that parasomnia and its associations are syndrome specific and more related to executive functioning than anxiety in the clinical groups, and more related to anxiety in the TD group. Previous studies assessing the relationship between psychological outcomes and parasomnia have tended to associate them with behavioural and affect related outcomes. According to Wengel and colleagues (2011), parasomnias were significantly correlated with behavioural outcomes of the Sensory Profile (Spearman Correlation =0.52, p=0.05). Parasomnias are reported to be prevalent in up to 83% of individuals with Autism (Ming, Sun, Nachajon, Brimacombe, & Walters, 2009) but with mixed reports about its relationship with psychological outcomes, depending on subjective and objective report. One PSG study conducted by Ming and colleagues (2009) examining parasomnia in children aged between 3-12 years with diagnoses of Autism (n=23) found that whilst parasomnias were prevalent in their sample, they were not associated with anxiety or mood instability. Meanwhile, in the previously mentioned study by Gunes and colleagues (2019), parasomnia as measured by the CSHQ was significantly related to CARS score. In the TD population, parasomnias are associated with fatigue, emotional stress, separation anxiety, bullying or fear/ worrying (Wolke & Lereya, 2014), anxiety and related psychopathology (Meltzer & McLaughlin Crabtree, 2015).

2.9.2.7 SDB

SDB was associated with Anxious symptoms in the FASD group, and several anxiety and behavioural subscales in the TD group but not significantly associated with any psychometric data in the Autism group. Sleep disordered breathing was not significantly higher in the clinical groups than the TD group. these findings are supported by previous studies: neither Chen et al. (2012) or Wengel et al. (2011) found significant differences in SDB between FASD participants and typical controls when measured by CSHQ. However, pulse oximetry data reveals that children with FASD (in particular those with FAS craniofacial characteristics) have increased levels of SDB, which may account for the shorter sleep

durations and night wakings, but are not accurately identified by caregiver report. This is one of the limitations of using caregiver reported data, rather than objective data and is an important limitation of this study. In the CSHQ, SDB is measured on the basis of three questions: child grinds teeth; child snores; child snorts or gasps during sleep. These cannot always be known especially with older children who tend to become more independent with bedtimes and wake times. Another limitation of this study is the lack of factor validity on the subscale of SDB in the CSHQ. Whilst Markovich and colleagues (2015) found that sleep onset delay, sleep duration, night waking and SDB subscales were around 80% in accordance with PSG (Markovich et al., 2015), and Holley and colleagues (2010) found that parental reports of sleep duration were significantly correlated with actigraphy measures, factor validity of the CSHQ would ensure more accurate reporting of sleep problems.

Two interesting findings were revealed on the subscale of SDB. Firstly, SDB scores between FASD and Autism were significantly similar, as were their associations with anxiety, executive functioning and behaviour. Secondly, significant correlations appeared to cluster around SDB in the TD population, where it was strongly related to nine anxiety and behaviour subscales, as well as the SCAS and CBCL totals. This concurs with previous data on SDB in TD populations, in which negative behavioural and affect related outcomes are associated with respiratory events (Mietchen et al., 2016).

2.9.2.8 Daytime Sleepiness

The CSHQ measures daytime sleepiness across eight questions asking whether the child wakes up by themselves, appears to be sleep or falls asleep in various relaxed daytime activities and difficulties waking up in the morning and becoming alert. Daytime sleepiness was significantly higher in the clinical groups than the TD group, with children with FASD showing the highest levels of daytime sleepiness out of the three samples. This is in agreement with previous CSHQ assessments in the FASD population (Chen et al., 2012, Wengel et al., 2012), however the study conducted by Wengel and

colleagues (2011) did not find any significant correlational data between levels of daytime sleepiness and sensory issues.

Children with Autism were more likely to engage in aggressive and delinquent behaviour if they were sleepy during the day. Similarly, children with FASD were more likely to have social problems if they were sleepy during the day. Whilst anxiety and behavioural symptoms were predicted by daytime sleepiness in the Autism and FASD groups, daytime sleepiness was a predictor of several behavioural, anxiety and executive functioning characteristics that appeared to cluster around the TD group but not the clinical groups. This is in line with previous research on behaviour and sleep in TD populations in which daytime sleepiness is associated with maladaptive behavioural functioning and school performance (e.g. Kelly, Kelly, & Sacker, 2013; Sadeh et al., 2002; Touchette et al., 2007). Daytime sleepiness can have several causes, but in TD children is increasingly the result of shortened sleep duration due to the pressures of school, increased usage of electronic devices and blue light (Hanifin et al., 2019). There is a need for further research in this area to ascertain reasons for these sleep, behavioural and affect related outcomes.

2.9.3 The Spence Children's Anxiety Scale (SCAS)

As predicted, children with Autism and FASD had significantly higher levels of anxiety, in both total and subscales of the SCAS (panic, separation anxiety, physical injury fears, social phobia, obsessive compulsive, generalised anxiety). Regression analysis revealed that a significant proportion of anxiety problems in the Autism, FASD, and TD groups was attributable to sleep problems, apart from in the generalised anxiety and obsessive-compulsive subscales. There additionally appeared to be age, sex and SES related differences between the three groups, which could significantly predict anxiety.

Children with FASD displayed more 'worry' based anxieties, whilst children with Autism displayed more 'fear' based anxieties. On the other hand, both clinical groups also shared significant similarities, so it is unclear whether anxiety profiles are syndrome specific or whether they overlap (Figure 2.9).

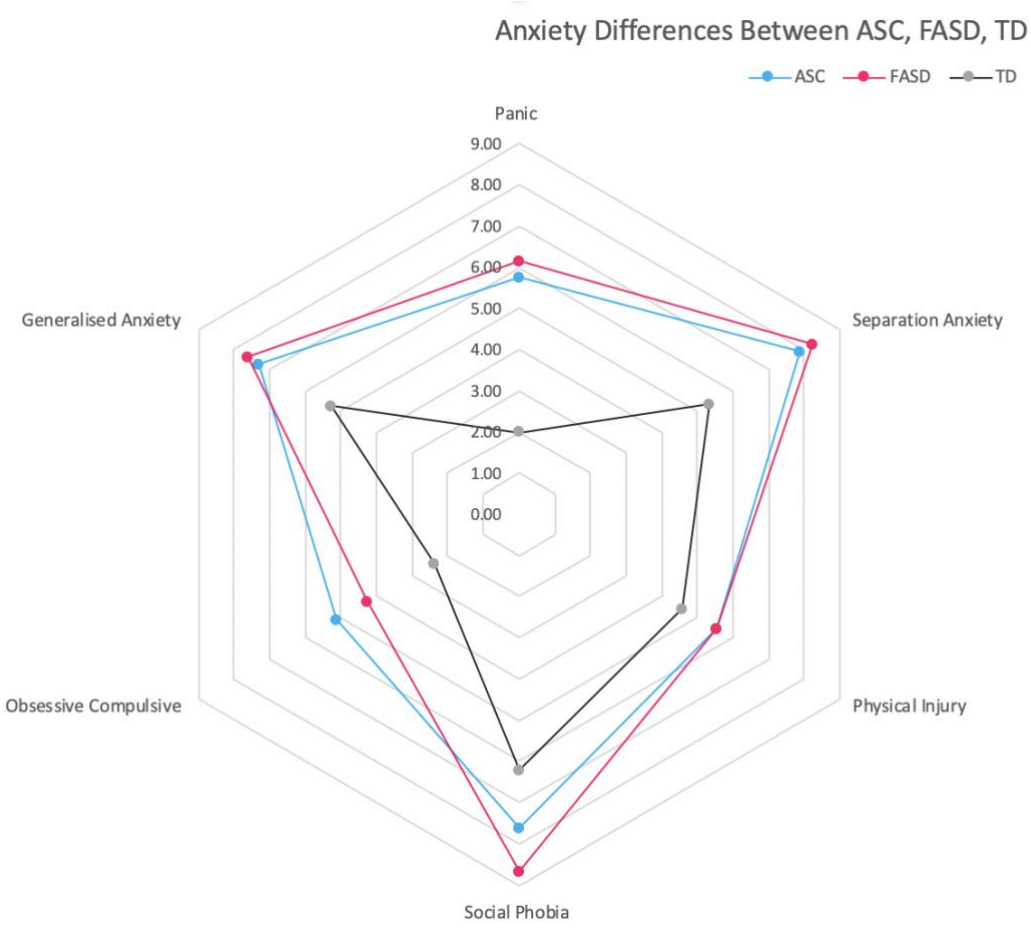


Figure 2.9: Radar Chart showing SCAS raw score differences between the three groups

Sleep problems predicted panic, separation anxiety, physical injury fears, social phobia and SCAS total scores in the Autism, TD and FASD groups. Unexpectedly, sleep did not significantly predict generalised anxiety and obsessive-compulsive symptoms in the Autism or FASD groups, but did in the TD group. There were significant differences between Autism/TD and FASD/TD on both the generalised anxiety and obsessive-compulsive scales, and in both scales the mean scores for the clinical groups exceeded the clinical cut-off points. However, this did not correlate with sleep as strongly as in the TD group. To my knowledge, there are two previous studies looking as SCAS and sleep in populations with Autism (May, Cornish, Conduit, Rajaratnam, & Rinehart, 2015; Rzepecka et al., 2011), and none in FASD populations. Both previous studies report the outcomes of total SCAS scores and their associations with sleep variables, rather than the associations between subsets.

Previous studies on sleep and anxiety in TD populations have noted Generalised Anxiety symptoms as being the most associated with sleep disturbances (e.g. Alfano, Zakem, Costa, Taylor, & Weems, 2009; Fletcher et al., 2018; Gregory & Eley, 2005). It is interesting that both FASD and Autism groups had similar outcomes in relation to generalised anxiety, obsessive-compulsive symptomology and sleep. This may support the idea maintained by Factor and colleagues (2016) that anxiety symptomology in Autism is a product of repetitive and restricted behaviours that are not necessarily associated with worry or fear – compulsive stimming, for example can feel positive and calming in a child with Autism, whilst compulsive hand washing or ritualistic behaviour in a TD child might be the result of altered perceptions based in fear and worry (Factor, Condy, Farley, & Scarpa, 2016).

Sleep and affect related outcomes such as anxiety and depression are part of a complex bidirectional relationship combining multiple psychological and sensory domains. It may equally be said that insomnia is a diagnosis with depression as an outcome – or that depression is a diagnosis with insomnia as an outcome, with no definitive conclusions been made regarding the two (Alvaro, Roberts, & Harris, 2013; Litwiller, Snyder, Taylor, & Steele, 2017). Such relationships may exist in the present study sample; anxiety caused by environmental cues may be driving sleep onset delays, but short sleep duration in turn may be contributing towards negative affect experienced in the daytime. When additional factors such as school performance, negative home experiences or social anxieties are also present, such a bidirectional relationship can be more pronounced. Further analysis of this would be warranted through experimental and objective studies in Autism and FASD populations, particularly assessing the differing consequences of sleep onset delay and sleep duration.

Failure to fall asleep and stay asleep, when driven by persistent anxious ruminations, can consist of several neurochemical processes in the TD population, but may be exacerbated in FASD and Autism populations due to differences in neurological functioning. Sleep-wake regulation results from circadian and homeostatic processes. These include sleep inducing inhibitors (such as the neurotransmitter GABA) and wake and arousal mechanisms including (among many others) the

neurotransmitter CRH (Corticotropin Releasing Hormone), the LC-AN (Locus Cereleus- autonomic nervous) System, and the HPA (Hypothalamic Pituitary Adrenal) Axis. These mechanisms are involved in a feed-forward system which respond to environmental and physiological stresses, but are vulnerable to dysfunction. Therefore, neurochemical reactions to environmental and physiological arousals can proceed even when the stressful situation is removed. Acute stress, mediated by CRH and HPA Axis mechanisms, can manifest in changes in both NREM and REM sleep, and contribute to spontaneous waking even without stressors (Staner, 2010). This can be seen in the spontaneous waking experienced by individuals with anxiety symptoms, in particular with Panic Disorder, Separation Anxiety and Social Phobia. In the present study, significant associations were found between symptoms of Panic and sleep disturbances in both the TD and FASD groups. Panic Disorder symptoms include autonomic occurrences with increased psychic anxiety including palpitations, sweating, shortness of breath, paresthesia, or chest pains. Individuals with a diagnosed Panic Disorder are more likely to experience nocturnal panic attacks, sleep paralysis, apnea, sleep terrors, or nightmares, with or without environmental cues (Staner, 2010). The SCAS measures panic symptoms from questions such as “My child suddenly starts to tremble or shake when there is no reason for this”, “All of a sudden my child feels really scared for no reason at all” or “My child worries that (s)he will suddenly get a scared feeling when there is nothing to be afraid of”, which both fits the neurobehavioural profile of a dysfunctional HPA axis (Wieczorek, Fish, O’Leary-Moore, Parnell, & Sulik, 2015) and can explain elevated scores in items such as sleep latency and night waking. Prenatal alcohol exposure, mediated by negative early life experiences, alters the developmental programming of the HPA axis in children with FASD (McLachlan et al., 2016). Concomitantly around 91% of children with FASD have a co-occurring mental health condition, 20% of children with FASD will experience panic symptoms at a clinical level (Pei et al., 2011), while up to 40% of individuals with Autism experience panic symptoms (Stahlberg 2004). It was predicted that children with Autism and FASD would exhibit significantly higher anxiety and sleep problems than TD children, and that both groups would have significant associations with anxiety scores. Thirty nine percent of the variance in the Autism

SCAS/CSHQ composite score, 32% of the variance in the FASD SCAS/CSHQ composite score and 40% of the TD SCAS/CSHQ scores were attributable to disordered sleep after controlling for age, SES and sex. This supports previous studies in anxiety and sleep in TD and Autism populations and serves as an evidence base for the association between sleep and anxiety in children with FASD.

2.9.4 The Behavior Rating Inventory for Executive Functioning (BRIEF)

The neocortex is responsible for processing complex information associated with higher order processing and executive functioning. For example, Bilateral Magnetic Apraxia, or 'utilisation behaviour', can demonstrate what happens to social or impulsive behaviour in the event of neural damage to prefrontal areas. Individuals with utilisation behaviour respond to visual stimuli (usually objects) by involuntarily (or impulsively) reaching out, grabbing them, and using them for their intended purpose without it being socially appropriate to do so. Upon seeing a toothbrush nearby, an individual with frontal lobe damage may pick it up and start using it, even if they were in a supermarket at the time. There is a phylogenetic reason for this. Neuroanatomical compositions of the higher mammals include 'extra' neocortical matter in the prefrontal lobes which allow the understanding of social context to be applied to behaviour. This means that typical human behaviour is no longer entirely stimulus driven or environmentally dependent. So, when disinhibition or impulsivity occurs, it is an indication that there is a structural or functional atypicality in the prefrontal area (Bowman, 2016). Atypical brain development that is specific to both Autism and FASD is predominantly (but not entirely) associated with the prefrontal cortex and therefore executive functioning is a vital component of FASD and Autism. This section of the study aimed to both characterise the executive functioning profiles of FASD and Autism alongside each other and compare the sleep/executive functioning coefficients between groups. With this in mind, a visual representation of the results displayed above is shown in Figure 2.10.

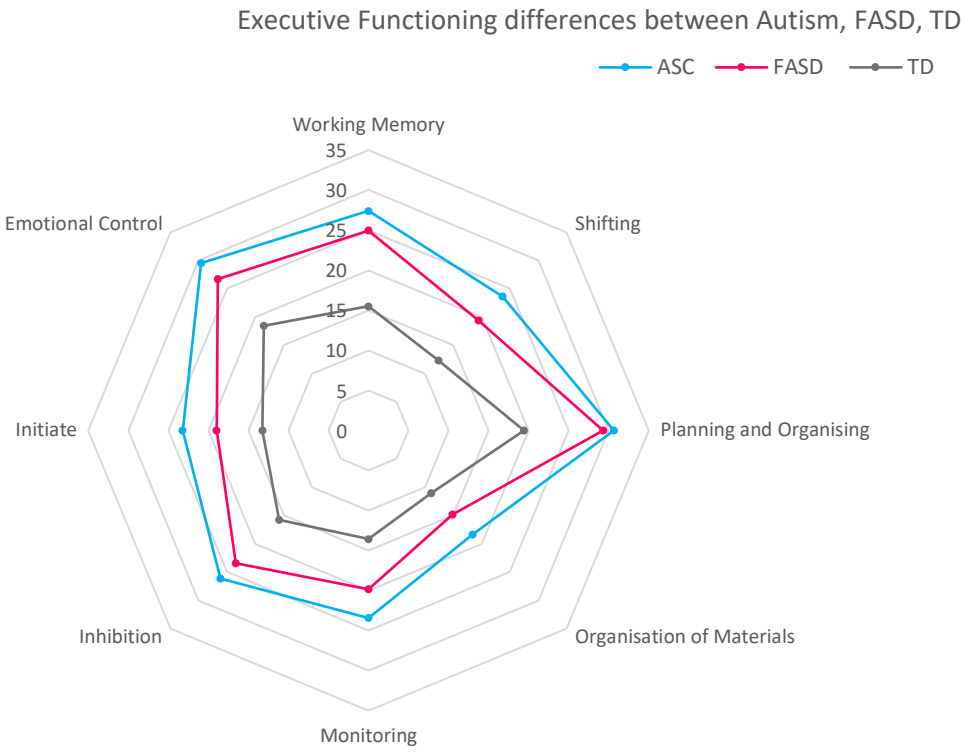


Figure 2.10: Radar chart showing BRIEF raw score differences between the three groups

The executive functioning differences in Autism, FASD and TD appear more amplified, in the order of TD<FASD<ASC, but fall within similar patterns. These results are in accordance with previously reported executive functioning results in FASD (Raja Mukherjee, 2019) and Autism (Hill, 2004) in which BRIEF subset scores were at clinical levels in all domains. However, this is the first time executive functioning profiles of FASD and children with Autism have been compared with each other. In Autism, enlarged frontal areas mature at a higher rate in early childhood and decline in volume after around 10-15 years of age (Ha, Sohn, Kim, Sim, & Cheon, 2015). Frontal area functioning is additionally associated with FASD, as well as ADHD, Obsessive Compulsive Disorder, Tourette's Syndrome, and Schizophrenia (Bowman, 2016), all of which are associated with atypical executive functioning.

Children with FASD often have elevated problems in executive functioning which become apparent when school routines and tasks become overwhelming (Mukherjee, 2019). In school settings, these

elevated problems however tend to become overlooked or attributed to maladaptive behaviour, since they may not appear to be syndromic or resemble more well-known neurodevelopmental conditions such as Autism or ADHD. The results here may offer an insight into why this is the case. Within these results, FASD executive functioning profiles do not exceed the levels of Autism executive functioning profiles and within a classroom might not look as clinically relevant or as urgent as the Autism profile. It may also be the case that FASD and Autism profiles look clinically similar, but the underlying neurobiological functioning differs. This supports previous work on the neurological differences between FASD and Autism, which maintains that whilst Autism may be the result of neural local overconnectivity and global underconnectivity, FASD is the result of functional impairment due to structural damage (Fletcher-Watson & Happé, 2019; Lange et al., 2017).

It was predicted that the two clinical groups would score higher in executive functioning domains than the TD group. This was found to be the case. Thirty one percent of the variation in scores in the Autism group, 36.1% of the variance in scores in the FASD group and 36.2% of variance in the scores in the TD group were attributable to sleep disturbances. This suggests that executive functioning profiles in Autism and FASD may be syndrome specific and that there is evidence that, according to caregiver report, executive functioning is associated with sleep disturbances in all three groups.

2.9.5 The Child Behaviour Checklist (CBCL)

Behaviour is the result of a complex interaction between executive functions, environmental stimuli and emotional responses (Bowman, 2016). For those working with children with FASD, there are more clinical and educational resources for externalised, aggressive and conduct related behaviours than internalised or withdrawn behaviours, most probably because the externalised behaviours warrant more immediate responses from caregivers and educators (Catterick & Curran, 2014). For this reason, most prior research on FASD and behaviour has focussed on externalised behaviours. The behavioural profile of Autism is more established, and less variable than the FASD behavioural profile; yet as can be seen in Figure 2.11 there appeared to be to be syndrome specific behavioural characteristics in both FASD and Autism.

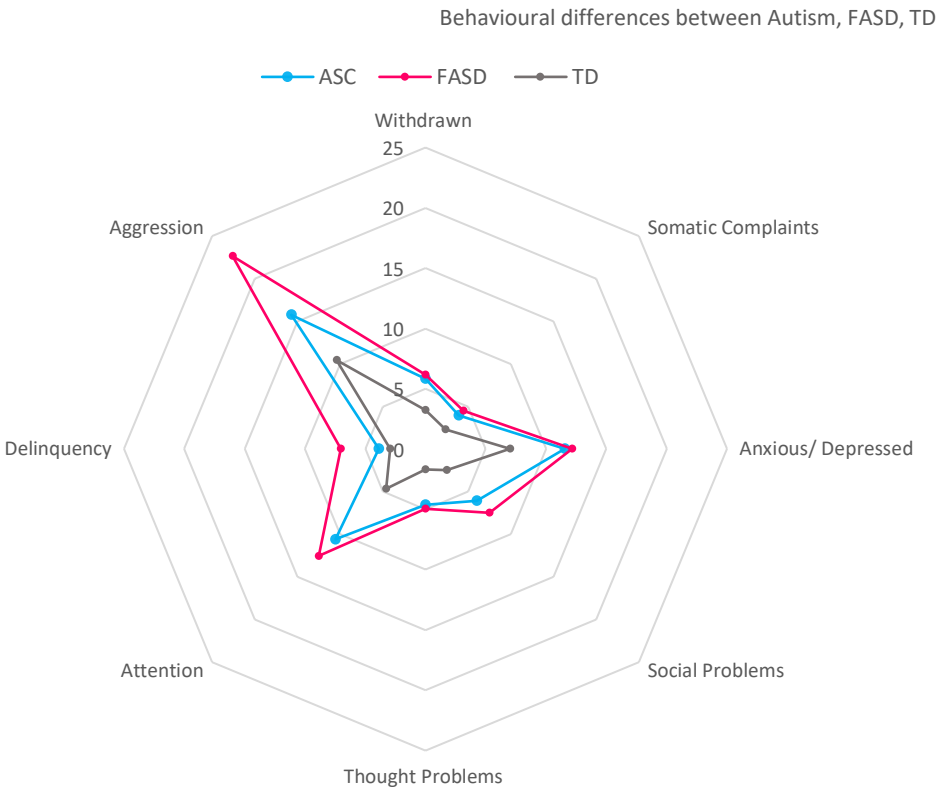


Figure 2.11: Radar chart showing CBCL raw score differences between the three groups

Emotion, memory and cognition all participate in the process of informing adaptive behaviour, in part by allowing meaning to be given to experiences, which are then used to influence and guide behaviour (Bowman, 2016). However, it is a commonly held belief, particularly in educational institutions, that reason and emotion are antithetical. In the UK, academic curriculums are based on traditional beliefs that stress reason and logic as part of attaining an academic goal, whilst 'non cognitive skills' such as emotional awareness can be taught through Personal, Social, Health and Economic (PSHE) curriculums. This dualist perspective is incongruent with neurobehavioural evidence that 'rational' behaviour is in fact the result of a complex association between memory, emotion and executive control, and that the idea of 'non cognitive' skills as 'emotional' skills is paradoxical. This is why the three aspects of anxiety, executive functioning and behaviour were chosen for this study. They make up what is described by Bowman (2016) as a 'new paradigm' where emotion plays a role in the decision-making process and allows individuals to choose between various options. This seems an appropriate set of variables with which to begin an exploration in neurodevelopmental conditions.

Figure 2.8 is a visual representation of the differences between behaviour subsets in the three groups. Previously (in Figure 2.7) children with FASD appeared to have lower levels of executive functioning difficulties, but here appear to present with higher levels of behavioural difficulties, with marked differences in aggression and delinquency. This was expected given the high number of children with FASD that present with conduct problems and is in agreement with previous studies comparing FASD and Autism characteristics (Stevens et al., 2013).

Levels of withdrawn behaviour were significantly similar in FASD and Autism groups and higher than the TD group. In both clinical groups, around 20% of children scored above the clinical cut off for Withdrawn behaviour whereas this was only true in around 5% of the TD group. Internalised behaviour tends to become overshadowed by externalised behaviour, especially in caregiver reports which may reflect behaviour that features more heavily in everyday parenting strategies. Nonetheless, it is important to point out that in both FASD and Autism groups, withdrawn levels were significantly

higher than the TD group, but not to the same extent as other behavioural symptoms. This is surprising given that 'rather be alone' and 'keeps to him/herself' seem to form part of the core behavioural profile of Autism. There were also unexpected sex related differences with boys scoring significantly higher than girls in the Autism group, and expected age-related differences with levels of withdrawn behaviour increasing with chronological age. Whilst the age related differences were to be expected, sex related differences might offer an interesting insight into whether individuals with Autism may experience social, gender and sex roles differently.

TD children with higher parasomnia and daytime sleepiness scores were more likely to be withdrawn in the daytime. This was not the case for the Autism or FASD groups. Confused arousals, sleep terrors or nightmares can be the result of underlying anxieties or disorders of affect, and it may be the case that other related psychopathological risk factors contribute to parasomnias in the TD group. Sleep problems were not significant predictors of somatic complaints in the clinical groups but were in the TD group. Typically developing children who experienced more night wakings, SDB and daytime sleepiness were more likely to present with somatic complaints. This is in line with previous studies, for example one cross sectional study conducted by Mulvaney and colleagues (2006) in a sample of school-aged children (*n*=403) found that, according to PSG and CBCL data, somatic complaints were significantly associated with SDB (Odds Ratio=3.33, *p*=0.017). One possibility for this was that SDB can often result in headaches, which is accounted for in the clinical assessment of SDB.

Parasomnias were predictors of social problems in the FASD and TD groups, whereas sleep duration was a predictor of social problems in the Autism group. Social problems are clinically reported in both children with FASD and children with Autism. Children with FASD tend to behave in a socially inappropriate manner and can present with delinquent, oppositional and defiant behaviour, whereas children with Autism tend to present with socially unaware behaviour. Both groups tend to have atypical social functioning that presents in different ways (see Sections 1.2 and 1.3). This concurs with previous research on sleep and social behaviour in Autism. One narrative review for example,

conducted by Devnani and Hedge (2015) reports that sleep time corresponds to increases in Autism behaviours, including social interactions. Parasomnias, which are an indication of an underlying neuropathology, were predictors of social problems in the FASD and TD groups. Although further research is needed in this area, this could perhaps be due to social fears in the daytime reflecting in nightmares. One qualitative study that supports this theory in both FASD and TD populations was conducted in 2018 by Spruyt and colleagues. In this study, sleep complaints were qualitatively analysed through text mining, finding that nightmares and school based fears were amongst the most used words amongst caregivers of children with FASD (Spruyt et al., 2018).

It was predicted that children with FASD would have significantly higher socially maladaptive and aggressive problems than children with Autism, and that children with Autism would present with a higher number of social and communication difficulties than children with FASD. This was based on the hypothesis that the social and communication phenotype is more identifiable in the Autism population, and based on previous factor analysis of the CBCL, social and aggression problems were considered to be part of the neurobehavioural profile of FASD. Delinquency scores were significantly higher in the FASD group than the TD group, with no difference in scores between the Autism and TD groups. Contrary to prediction 3 ('*Children with Autism will present with a higher number of social and communication difficulties than children with FASD'*), children with FASD had significantly higher social problems than the Autism group. According to caregiver report, 33% of the variance in Autism behaviour scores, 25% of the variance in FASD behaviour scores and 45% of the variance in TD behaviour scores were attributable to sleep problems. This is in agreement with previous research on the positive linear association behaviour and sleep in Autism and TD populations and provides evidence that sleep and behaviour may be related in the FASD group.

2.9.6 Limitations

Several limitations have been reported within this discussion that can be summarised as follows: Parental reports are subjective views of children's behaviours and further analysis can benefit from objective sleep measures such as actigraphy or PSG; furthermore the instrument used within this study to measure sleep could benefit from further validation studies or development. This study may contain selection bias in that parents of children with sleep problems were more likely to want to take part and the present sample may not have the heterogeneity of a population-based sample. Predictions within this study are statistical descriptions. Without an experimental design and with the limits of cross-sectional data, causation cannot be implied. However, this study has provided a platform for the need for further examination using objective sleep and cognitive measures in this clinical population.

2.9.7 Summary

This is the first study to show how sleep disturbance predicts anxiety, behaviour and executive functioning in children with FASD and Autism. Within the three groups, significant regressions were found associating sleep with several psychological domains that may be amenable to treatment. In the clinical groups, sleepy children were more likely to engage in delinquent and rule breaking behaviours while in the TD group, sleepy children experienced a large number of social, behavioural and affect related outcomes. On the other hand, children in the Autism and FASD samples who slept less were significantly more likely to experience a large number of executive functioning, anxiety and behavioural problems, whilst this was less pronounced in the TD sample.

This is the first study to analyse anxiety, executive functioning and behaviour profiles of a large number of children with Autism and FADS side by side. The present results reveal an interesting pattern of syndrome specific as well as syndrome-similar results that should be further studied in order to explore the vast array of the consequences of prenatal environments, and the neuropathological profiles of conditions related to frontal lobe functioning.

This study aimed to investigate the theory that behaviour is the manifestation of executive control and affect related processes, and that this triad of processes is mediated by sleep. As predicted, many anxiety, executive functioning and behavioural outcomes were significantly related to sleep. All neurodevelopmental, depressive, dissociative and psychotic disorders are at some point underpinned by executive, social, behavioural and affect related processes and further investigation in this field should come from such assessments of not only Autism and FASD, but across the range of other conditions for which these domains are compromised, and the extent to which sleep can mediate or ameliorate these processes.

Given the importance of sleep to healthy neurodevelopment there is a pressing need for sleep intervention studies in these populations. Sleep disturbances can often be overlooked or assumed to be intrinsic to the neurodevelopmental condition rather than amenable to treatment. Early identification and intervention for sleep problems should be a therapeutic priority, supported by research to assess whether improvements in sleep are associated with improved cognitive and behavioural outcomes, including reduced anxiety.

Chapter 3

3.1 Study 2: Sleep and cognition in Autism and FASD

The purpose of this thesis is to support the evidence that psychological domains are mediated by sleep processes. As discussed in the literature review (See Sections 1.1.4-1.1.4.3), an underlying assumption is that, in childhood, one function and role of sleep is to aid in the neurodevelopmental process. Study 1 of this thesis examined the linear associations between sleep and behavioural, executive functioning and affect-related processes, and found evidence of distinct relationships between sleep and these domains in TD children, children with Autism and those with FASD. Not only were these relationships apparent within the three samples, but they appeared to be both syndrome specific in some areas and significantly similar in other areas. The second study of this thesis used objective methodology to measure sleep and cognition in a sample of TD children (*n*=45), children with Autism (*n*=21) and those with FASD (*n*=29). The domains of working memory and attention were examined using Digit Span and Choice Reaction Time (CRT) task, since these domains work in communication with each other (Bowman, 2016) and are known to be mediated by sleep in both TD populations and those with neurodevelopmental conditions (Kamara & Beauchaine, 2019). Tests of verbal and nonverbal MA were conducted using the Ravens Standard Progressive Matrices (RSPM) and British Picture Vocabulary Scale (BPVS) with the intention of providing a developmental account of sleep and cognition profiles in children. This chapter begins with a review of the literature on sleep, working memory and attention in Autism and FASD. The aims and hypotheses of this study, its methodology and results follow. A discussion of statistical associations, limitations and outlines for areas of further research concludes this chapter.

3.2 Introduction

3.2.1 Working memory

Working memory is a limited capacity cognitive system which is responsible for temporarily holding information for the purposes of higher order processes such as reasoning, behaviour, decision making and other such attention demanding tasks (Holdnack, 2019). A widely used model of working memory formulated by Baddeley and Hitch (1974) theorises its three functional components: the phonological loop (which keeps auditory information immediately available), visual sketchpad (which keeps visual and spatial information immediately available), and central executive (which allocates cognitive resources to manipulate the immediately available information). These short-term functional components interact with long-term memory in order to retrieve previously learned information, which can then either be used in the process of higher order functioning, process new information for long-term storage, or be lost from the short-term storage. In typical development, working memory capacity increases gradually during childhood and declines gradually in adulthood (Schweppe & Rummer, 2014). Neo-Piagetian theories maintain that if processes of central executive control feature as a mechanism to working memory capacity, they are key to the cognitive function of learning, and therefore working memory capacity is fundamental to the mechanistic process of atypical neurodevelopment (Alloway & Gathercole, 2012; Holdnack, 2019).

Improvements can be made to working memory performance through repetitive tasks and training, even in populations in which memory is declining. In one randomised controlled trial conducted by Huntley and colleagues (2017), working memory training based on 'chunking' significantly improved phonological memory and general cognitive function in a sample of patients (*n*=30) with early onset Alzheimer's disease (Huntley, Hampshire, Bor, Owen, & Howard, 2017). Sleep can accelerate this process and working memory performance can be improved further by both training and periods of sleep. In one study by Kuriyama and colleagues (2008), a sample of healthy adults (*n*=29) were administered a spatial variant of the *n*-back working memory task; task performance was significantly

improved after post-training sleep (Kuriyama, Mishima, Suzuki, Aritake, & Uchiyama, 2008). Similarly, in a randomised controlled trial conducted by Hiscock and colleagues (2015) with children with a diagnosis of ADHD (*n*=244), working memory as measured by digit span tests improved after six months of sleep hygiene and behavioural interventions (Hiscock et al., 2015). As outlined in Section 1.1.4.3, SWA, NREM and REM serve what are thought to be specific functions contributing to declarative, episodic and procedural memory consolidation. The previously mentioned studies conducted by Huber (2004) and Barakat et al. (2011) found that memory tasks correspond with SWA and sleep spindles, for example motor tasks result in SWA in the motor control regions of the brain. Conversely, it has been theorised that sleep would increase as a result of increased information processing during the day. When Quach and colleagues (2018) conducted a series of randomised controlled trials in school aged children (*n*=452), conversely, they found that sleep duration did *not* change in correspondence with increased working memory tasks during the day. This points to the importance of distinguishing the difference between sleep architecture and sleep duration in such studies, since SWA was not known in this study, rather was assumed by increases in sleep duration (Quach, Spencer-Smith, Anderson, & Roberts, 2018).

In children with FASD, PAE is associated with the inhibited growth, structure and function of prefrontal and parietal areas which are responsible for working memory processes. Research on working memory in children with FASD consistently describes problems in this neuropsychological domain, both in psychometric testing and fMRI research (For reviews see: Khoury et al., 2015; Lange et al., 2017; Rasmussen, 2005). Perhaps because of the paucity of data in this field, many of these studies set working memory within a battery of standardised tests, and so where working memory nestles within other neuropsychological domains, such as executive functioning (Khoury et al., 2015), mathematical ability (Rasmussen & Bisanz, 2011), visuospatial and oculomotor control (Paolozza et al., 2014), and attentional capacity (Boseck, Davis, Cassady, Finch, & Gelder, 2015), these relationships are well understood. This may lead us to believe that the working memory profile of a child with FASD

sits neatly within the Baddeley and Hitch model, since impaired working memory capacity in this population works in communication with impaired phonological and visuospatial processing domains. However as will be discussed below, children with FASD can present with working memory difficulties but might at times have some sustained attentional capacities that are on par with neurotypical children. Perhaps this suggests that within the Baddeley and Hitch model, working memory needs all three domains functionally intact in order to function to a typical level. Furthermore, there is evidence suggesting that working memory can be improved with rehearsal training in children with FASD. In one study conducted by Loomes and colleagues (2008), a sample of school aged children with FASD (*n*=33) were trained to rehearse working memory techniques by whispering digit spans that were read aloud to them. In this study, working memory significantly improved for the experiment group but not for the control group, which not only suggests that working memory can be improved in this population but should also be an area for educational interventions given the importance of working memory to learning outcomes (Loomes, Rasmussen, Pei, Manji, & Andrew, 2008). Nonetheless it is clear that diminished working memory capacity is intrinsic to FASD. Astley and colleagues (2009) conducted fMRI assessments on a sample of children with FASD (*n*=58), whilst administering the *n*-back working memory task, in which amongst a series of faces that were presented, participants were required to identify duplicate consecutive and non-consecutive images. Performance was poorer in the FASD sample than control sample, and performance on the task was marked by significant deficits in long-range prefrontal, posterior and parietal lobe function (Astley et al., 2009). Together these cognitive and functional neuroanatomical studies suggest working memory problems are intrinsic to the FASD neurocognitive profile.

In individuals with Autism, working memory is often conceptualised as a process sitting within the broader domain of executive functioning, and therefore integral to the cognitive processes that make up the Autism profile. Decreased working memory in Autism is associated with decreased social communication functioning, increased RRBI's (Barendse et al., 2013), learning paradigms (Alloway &

Gathercole, 2012), behavioural regulation, and attentional control (Hughes et al., 1994). Similarly to FASD, working memory is therefore regarded as an integral part of the cognitive features of Autism. In a meta-analysis performed by Habib and colleagues (2019), 34 studies were identified assessing working memory processing in individuals with Autism across the lifespan. Across the studies, individuals with Autism scored significantly lower in visuospatial working memory than control participants. This was the case in both adult and child (aged 11-18) populations that were included in this meta-analysis, and accounted for the differences in methodological assessments of working memory, as well as age and IQ (Habib, Harris, Pollick, & Melville, 2019). In assessing studies focussing on phonological working memory, the same meta-analysis found a heterogeneity in results but also found that scores on this aspect of working memory were consistently lower than controls. One limitation of the study mentions that the paucity of data here means that this difference in score should be interpreted with care, particularly given that the studies focussed on adults, and in adulthood working memory tends to decline (Habib et al., 2019). Earlier work suggests that phonological working memory in children with Autism is more consistent with TD controls. Mottron and colleagues in a 2001 review claimed that children with Autism encode phonological information at higher levels than TD children, since the difference lies in episodic memory and lexical and semantic attributes. This review, which used studies that were not included in the meta-analysis conducted by Habib et al. (2019), maintained that children with Autism exhibited typical performance in verbal immediate and serial recall tests of working memory, but scored lower in visuospatial and attentional components of working memory (Mottron, Morasse, & Belleville, 2001). The mechanistic processes of working memory in Autism are thought to be due to altered function in the frontal areas. FMRI studies such as those conducted by Yeung and colleagues (2019) show that when *n*-back tasks were administered to adolescents with diagnoses of Autism, compensatory mechanisms were employed in the right-lateralised prefrontal areas, that were not used by controls. This suggests that individuals with Autism may be employing a different visuospatial processing style to compensate (Yeung, Lee, & Chan, 2019).

In summary, working memory in Autism tends to be more compromised when serial recall carries specific meaning (such as lexical and semantic meaning) which may be difficult for an individual with Autism to decipher. In some areas, individuals with Autism may be compensating and recalling at the same rate as typical individuals, whilst in other areas they consistently score lower than typical controls.

3.2.2 Attention

Vigilant (or sustained) attention is the effortful, adaptive ability to maintain focus and remain alert to stimuli across a period of time and is a major component of cognitive processes and task performance (Hudson, Van Dongen, & Honn, 2020). In child development, attention is a critical aspect of learning, since it incorporates the ability to selectively attend to important stimuli whilst ignoring competing aspects of the environment. In the psychology literature, sustained attention tends to be measured with a continuous performance task (CPT), in which target signals across a computerised screen measure an individual's response rate, inhibition and impulsivity, response time, and ability to maintain vigilance. This performance ability sits within the context of Signal Detection Theory, a widely used model that places deficits in attention amongst the ability to discriminate between 'target' and 'noise' (Green & Swets, 1966). In addition, attention tasks must also take into consideration an individual's willingness (as well as ability) to respond. Theories around why deficits in vigilance occur take into consideration issues such as boredom or under stimulation (Manly, Robertson, Galloway, & Hawkins, 1999), neural habituation to repeated stimulations, altered salience and cognitive control (Tegelbeckers et al., 2015) and cognitive fatigue (Pattyn, Neyt, Henderickx, & Soetens, 2008).

Prenatal alcohol exposure is associated with reduced vigilance, inattention and impulsivity in children. One of the diagnostic features of FASD is reduced attention, and its neurocognitive profile includes hyperactivity, distractibility, impulsive behaviour and slower reaction times in attentional tasks (Rangmar, Sandberg, Aronson, & Fahlke, 2015). For this reason, children are at times diagnosed with

ADHD and FASD in parallel (Kooistra, Crawford, Gibbard, Kaplan, & Fan, 2011). One early but robust study found evidence for the extent of attentional atypicalities in this population and their association with PAE. At one timepoint during a longitudinal study conducted by Streissguth et al. (1996), a CPT was administered to a cohort of children with PAE (*n*=473). Within this sample, after confounding effects such as environmental conditions, demographics, presence of other prenatal teratogens and maternal stress were controlled for, the frequency and timing of PAE was most associated with errors of omission and commission, reaction time and errors in vigilance (Streissguth, Barr, Kogan, Bookstein, 1996). More recently, tests of attention on children with FASD have tended to focus on the delineation between FASD and ADHD. Whilst there is a diagnostic overlap and several similarities between the two conditions, clinical differences between FASD/ADHD and idiopathic ADHD are apparent in the areas of vigilance and reaction time, as well as distractibility (Kooistra et al., 2011). Additionally, children with FASD are less amenable to interventions designed for children with ADHD because of differences in processing and contextualising information (S. Lange et al., 2017). To this extent, Burden and colleagues (2005) found that children with FASD tended to find more difficulties than age matched controls in tasks involving effortful rather than automatic processing (Burden, Jacobson, Sokol, & Jacobson, 2005). Similarly, Roebuck and colleagues (2002) reported that individuals with FASD showed greater difficulty than controls on a task that involved interhemispheric transfer of information (Roebuck-Spencer, Mattson, Marion, Brown, & Riley, 2004). Thus, there is growing evidence that children with FASD have difficulty in rapidly processing relatively complex information. As will be discussed below, individuals with Autism show a diversity in attentional capacity, from distractibility to narrow attentional over-focus on one item or stimulus. In the Autism literature, it is now emerging that RRBIs and attentional capacity are better understood in terms of increased perceptual processing, rather than deficits in filtering or ability to maintain focus (Remington & Fairnie, 2017). One similarity between Autism and FASD is that both include repetitive behaviours, although in FASD this is more commonly framed as obsessional behaviour. Examples of this may include listening to the same song repetitively, pacing from one room to another for hours, or being absorbed in a video game for

prolonged periods of time, without stopping to eat or sleep (Catterick & Curran, 2014). In one systematic review conducted by Popova et al. (2016), Obsessive Compulsive Disorder was prevalent in between 8-30% of individuals with FASD (Popova et al., 2016), and in study 2 of this thesis, obsessive behaviour was prevalent in the sample. Although Obsessive Compulsive Disorder includes a wider and more abstract pattern of repetitive ideas, thoughts and behaviours, and is likely to be mediated by external inputs such as environmental stresses, it requires narrow attentional focus and a switch between internal and external attention (Stern et al., 2017). Further studies in the area of perceptual capacity in FASD would shed light on these attentional similarities.

Children with Autism tend to show atypical attention, including alternations in attentional capacities, such as disengagement, orienting attention away from stimuli, or increased capacity and focus on narrow stimuli (Ames & Fletcher-Watson, 2010). In one narrative review, Keehn and colleagues (2013) conceptualise attention in individuals with Autism as the product of a deficit resulting in atypical social communication, which contributes to the weak central coherence profile. In this review, Keehn et al. maintain that attentional deficits are formed of functionally independent networks comprised of alerting, orienting and executive control functionality (Keehn, Wagner, Tager-Flusberg, & Nelson, 2013). Atypical attentional function is noted in infants with a high likelihood of Autism, such as the younger siblings of children with an Autism diagnosis and may act as an early indicator. For example, Elsabbagh and colleagues (2009) found that disengagement and facilitation from central to peripheral stimuli took longer in their sample of 9-10-month-old siblings (*n*=19) of children with an Autism diagnosis (Elsabbagh et al., 2009). Conversely, socially related attentional capacities such as visual searching and novelty detection reveal attentional *superior* functioning. In an fMRI study by Gomot and colleagues (2008) assessing attentional functioning when presented with novel auditory stimuli, the authors found that frontal and parietal areas were hyper-aroused which led to faster reaction times than typical controls (Gomot, Belmonte, Bullmore, Bernard, & Baron-Cohen, 2008). More recently, Remington & Fairnie (2017) investigated auditory capacity when taxed with perceptual load,

finding that increased capacity simultaneously results in enhanced selective attention task performance, but also leads to increased distractibility when perceptual loads were lightened (Remington & Fairnie, 2017).

3.2.3 Sleep and cognition

Vigilant attention and working memory, as well as a range of cognitive processes, are affected by sleep deprivation (Hudson et al., 2020). One reason for this is the allostatic process of sleep which is observed through Process S and Process C (See Section 1.1.3). In a sleep deprivation study conducted by Doran et al. (2001), reaction times on a psychomotor vigilance task fluctuated with total sleep deprivation time (total time 88 hours) depending on homeostatic and circadian pressures. This supports the 'state instability' hypothesis in which it is claimed performance during sleep deprivation varies according to the influence of the sleep initiating mechanisms of Process S and Process C (Doran, Van Dongen, & Dinges, 2001). Attentional capacity is one component in a number of interrelated cognitive processes, including working memory, semantic encoding, motor action and planning (Habeck et al., 2004). In understanding the relationship between attention and sleep, it is important to place it amongst a number of cognitive processes that are organised together. Recent work by Whitney, Hinson and Nusbaum (2019) conceptualises the cognitive effects of sleep loss using a 'dynamic attentional control framework' theory, which proposes that there is a pattern of 'preserved' and 'compromised' cognitive functions that show no or variable decline after sleep deprivation. This variable task performance can be understood in terms of the influence of sleep deprivation on frontostriatal circuitry. The ability to maintain some task relevant information remains intact after sleep deprivation, whilst the ability to update task relevant information is affected by sleep deprivation, which can in turn mean heterogeneity in CPT performance after sleep deprivation (Whitney, Hinson, & Nusbaum, 2019). In fact, in paediatric studies, attentional outcomes as a result of sleep restriction are variable. In a study conducted by Sadeh et al. (2003), sleep restriction of an hour a night for three nights on a sample of children aged between 9 and 12 years (n=77) did not have

an impact on CPT performance and had variable effects on neurobehavioural functioning (Sadeh, Gruber, & Raviv, 2003). Similarly, in a study conducted by Fallone et al. (2001), experimental sleep extension and restriction in a sample of children aged between 8 and 15 years (*n*=87) to ten hours extension, and four hours restriction, did not affect performance on a visual attention CPT (Fallone, Acebo, Arnedt, Seifer, & Carskadon, 2001). It must be noted however that within these restriction studies sleep restriction was more successful to implement than sleep extension.

Previous research suggests that sleep may mediate attention and working memory in children with Autism. Al-Backer and colleagues (2018) measured sleep and attention in a sample of children with a diagnosis of Autism aged between 7 and 10 years (*n*=18). Actigraphy variables and a selection of CPTs from the Cambridge Neuropsychological Test Automated Battery (CANTAB) were administered, and results showed that those with shorter sleep duration had higher response times in motor and simple reaction time tasks (Al-Backer, Al-Backer, Alzawad, Habibullah, & Bashir, 2018). In one study assessing the association between sleep disturbances and digit span recall in adolescents with Autism (*n*=96), Calhoun and colleagues (2019) assessed whether insomnia and parasomnia symptoms, as measured by a subset on the Pediatric Behavior Scale (Lindgren & Koeppl, 1987) predicted working memory outcomes, as measured by the Weschler Intelligence Scale for Children (WISC-IV, Weschler 2003). In this study, children who were reported by their caregivers to have slept less than optimal amounts and experienced parasomnias such as sleep walking were more likely to score lower on tests of working memory (Calhoun et al., 2019). Conversely, in an earlier study by the same authors, but in infants and children between the ages of 1 and 15 years (*n*=477), across the Autism spectrum (IQs 9-146) sleep was not significantly correlated with working memory when using the same methodology (Mayes & Calhoun, 2009). The difference between the two sets of results may be due to the variations in the cognitive baselines of participants.

In a systematic review and meta-analysis on cognition and sleep in paediatric populations, Short et al. (2018) identified studies using objectively measured sleep duration and cognitive function in children

(Short et al., 2018). Overall, fourteen studies measuring working memory and sleep in children aged between 5 and 12 years (*n*=1568) revealed a homogeneity of variance (r=0.02, *p*=0.63). These studies utilised a diverse number of working memory tasks, including *n*-back tasks, digit span tests from the Weschler and Woodcock John tests of intelligence, word memory tests and symbol tapping tasks, as well as actigraphy or PSG. In the six studies included in the same meta-analysis assessing processing speed and sleep, five reported associations between attention and sleep, however with random effect size too small to be significant (r=0.05, *p*=0.4). As with other meta-analytic reviews, this variance can be attributable to the differences in methodology, but as the authors note, there may be instances when cognition is not linearly related to sleep. One reason for this may be the large numbers of covarying data that might influence sleep and cognition, which are not always accounted for in meta-analytic reviews. For example, one study included in the review examined the relationship between sleep and cognition in children using body mass, dietary intake, sedentary time and exercise as covariates. In this study, conducted by Hjorth et al. (2016), a linear relationship between sleep and reaction time was not found, but in the overall model, children with more sedentary lifestyles, higher body mass and sleep problems tended to have lower cognitive scores (Hjorth et al., 2016).

3.3 Aims and hypotheses

The aims of this study were:

1. To objectively measure and report on sleep quality and quantity in children with Autism, FASD and TD children.
2. To objectively measure working memory, attention, fluid intelligence and receptive vocabulary tasks in children with Autism, FASD and TD children.
3. To check for 'syndrome specificity" (i.e. statistically different scores than the other two groups) and compare group differences in sleep quality/ quantity, receptive vocabulary, fluid intelligence, working memory and attention in children with Autism, FASD and TD children.
4. To examine whether sleep duration and sleep efficiency are related to chronological and mental development in children with Autism, FASD and TD children.
5. To examine whether working memory, attention, fluid intelligence and receptive vocabulary are related to chronological and mental development in children with Autism, FASD and TD children.
6. To examine whether there are (or are not) significant regressions between sleep duration, sleep efficiency and sleep fragmentation and cognitive scores in children with Autism, FASD and TD children.
7. To compare subjective caregiver reported sleep data to objectively quantified actigraphy data.
8. To examine whether sex and SES are predictors of sleep and cognitive outcomes.

It is predicted that:

1. a) Children with FASD and Autism will have lower sleep duration and sleep efficiency, and higher sleep fragmentation than TD children (Díaz-Román et al., 2018; Inkelis & Thomas, 2018).

b) Sleep problems, as defined by sleep duration, efficiency and fragmentation, will be syndrome specific.

2. There will be age associated differences in cognition in children with Autism, FASD and TD children. It is expected that older children will perform better on cognitive tasks than younger children (Fletcher-Watson & Happé, 2019b; Novick Brown et al., 2012)
3. a) Children with Autism will score higher than children with FASD on cognitive tasks (Happe & Fletcher Watson, 2019).

   b) TD children will score higher than the clinical groups on cognitive tasks (Kodituwakku, 2009).

   c) Children with FASD will present with higher levels of attentional problems, in particular inhibitory control (Mukherjee et al., 2013)
4. There will be developmentally related changes in cognitive tasks in all three groups (Happe & Fletcher Watson, 2019; Kodituwakku, 2009).
5. Sleep and cognition will be linearly related in Autism, FASD and TD groups. The higher the sleep duration and sleep efficiency, the higher the cognitive ability (Inkelis & Thomas, 2018).
6. Caregiver reports on sleep will be inconsistent with objective measurements (Espie & Morin, 2012).
7. a) Sex will be associated with cognitive outcomes in all three groups. It is expected that girls will score higher than boys in cognitive measures (Corcoran, Crusius, & Mussweiler, 2011).

   b) SES will be associated with cognitive outcomes in all three groups. It is expected that those from higher SES will score higher than lower SES in cognitive measures (Corcoran, Crusius, & Mussweiler, 2011)

   c) SES will be associated with sleep disturbances in all three groups. It is expected that those from lower SES will have lower sleep duration and higher sleep fragmentation than higher SES (Corcoran, Crusius, & Mussweiler, 2011)

3.4 Power analysis

A-Priori analyses were carried out to assess necessary sample sizes and fit of data, as described in Section 2.3 earlier. For a power calculation of 0.8m, a sample size of 22 was calculated when assessing 2 variables (5 variables and covariables in total). This is outlined in Table 3.1.

Table 3.1: A-priori power analysis to check for sample size in Study 2.

F tests - Linear multiple regression: Fixed model, R^2 increase	
Effect size f^2	0.5
α err prob	0.05
Power (1-β err prob)	0.75
Number of tested predictors	2
Total number of predictors	5
Noncentrality parameter λ	*11*
Critical F	*3.63*
Numerator df	*2*
Denominator df	*16*
Total sample size	***22***
Actual power	0.8

3.5 Methodology

3.5.1 Ethical approval

Ethical approval for this study is outlined in Section 2.4.12.4.1

3.5.2 Participants

Participants were TD children and children with a diagnosis of FASD or Autism, aged between 6-12 years. This age group differs from the previous study and was chosen since it represents a large sample from which age-related changes in sleep and daytime functioning can be examined. All children had received either a diagnosis of FASD, Autism, or had no diagnoses. Screening tools for FASD and Autism (Neurobehavioural Screening Tool and Childhood Autism Rating Scale – Parents Version) were administered to ascertain children met diagnostic thresholds.

3.5.3 Exclusion criteria

In the Autism group, children were excluded if they had a diagnosis of a co-occurring neurodevelopmental condition. In FASD populations this is more difficult to ascertain, given the overlap of diagnostic criteria with other conditions such as ADHD or Sensory Processing Disorder. Only children with diagnoses of FASD and Autism were excluded so data would not overlap, however it was not viable to exclude other diagnoses given the overlap between FASD and other neurodevelopmental conditions. Given that in the UK the diagnosis of FASD includes an ADOS assessment, the FASD sample did not meet Autism diagnostic thresholds.

3.5.4 Recruitment

TD participants were recruited through a school in West London. FASD participants were recruited through the UK FASD Network mailing list, while caregivers of children with Autism were recruited through online Autism forums. Consent was gained from all caregivers, and assent gained from all children where this was understood. To avoid sample bias, this study was not explicitly advertised as a study of sleep, rather, it was advertised in different ways as a study on cognition, school and learning, home life, social and emotional behaviour and sleep (See Appendix for sample feedback booklets and recruitment material).

3.5.5 Participants

134 caregivers responded to the original study advertisements. Of these, 19 were excluded as they did not meet the diagnostic criteria (16 were children with PAE who did not have a FASD diagnosis from a clinical professional, 3 were children with Autism who had co-occurring diagnoses of ADHD). A further 4 were excluded as they did not meet the age criteria. Out of the remaining 101 families interested in taking part, 95 responded to further communication, signed consent forms and arranged to take part in the sleep and cognitive testing.

3.5.6 Sample

One-way between group ANOVAs indicated differences in age ($F(1,93)=1.06$, $p=0.03$, $\eta_p^2=0.09$), SES differences ($F(1,3)=1.06$, $p=0.04$, $\eta_p^2=0.08$) and differences between sex ($F(1,2)=6.58$, $p=0.01$, $\eta_p^2=0.02$). There were significantly more boys than girls in the Autism group, but no significant sex differences in the TD and FASD groups. Because of the heterogeneity of samples, all regression analyses were conducted with SES and chronological age (CA) as covariates. Regression analyses in the FASD and TD groups, additionally, contained Sex as a covariant, but not the Autism group. The final sample consisted of 95 participants, outlined in Table 3.2.

Table 3.2: Study 2 Participants

	Autism (n=21)	**FASD (n=29)**	**TD (n=45)**
Male/ Female	17/4	16/13	23/22
Age (M/SD)	8.42(1.81)	9.60(2.48)	8.12(1.29)
SES 1/2/3	5/15/1	1/20/8	6/29/10
Living with Biological parent	21	1	44
Living with Foster parent	0	22	1
Living with Adoptive parent	0	4	0
Living with Biological relative	0	2	0
Co-occurrence	0	SPD (*n*=2); ADHD (*n*=2)	-

3.5.7 Materials

This study used objective measurements to measure sleep, working memory, fluid intelligence, attention and receptive vocabulary.

3.5.8 Sleep measures

3.5.8.1 Actigraphy

Each TD child was given a CamNTech actiwatch 8 (CamNTech, 2019) to wear continuously for seven days and nights. Caregivers of children with FASD or Autism were given their child's actiwatch and

instructed to place the watch on the child's non-dominant wrist at bedtime, and take it off in the morning for seven consecutive nights, which ensured that watches were not taken off or lost during the day. Medical bracelets were placed on the watch instead of watch straps to ensure that the watch could not be removed during the night. All actigraphy data were collected during term time which ensured that sleep data reflected a normal school week. The watches were set to the default 'medium' sensitivity level and collected one-minute epochs of data.

3.5.8.2 Sleep diary

Caregivers completed a sleep diary recording bedtimes, waking up time, any naps or night wakings, and any unusual occurrences or activity (see Appendix). These bedtimes and wake times are reported in the sleep data as 'assumed' times, and are used as parameters to support the analysis of actigraphy data.

3.5.9 Experimental tasks

During the time in which children's sleep was being examined, a battery of tests examining cognitive performance was administered. All tasks were administered in semi-formal test conditions, with background noise similar to a quiet school classroom. In the clinical groups, caregivers were present either in the room or were nearby, and in the TD group testing took place in a small, separate room near a busy part of school. It was ensured that all children understood the tasks before progressing, and assent was acquired after the tasks had been explained by saying: "those are the games and activities that we are going to do today, how does that sound? Would you like to do that and do you have any questions?". Children were encouraged to concentrate on the activity but were offered the option of taking a break and returning if it seemed to be causing cognitive exhaustion. A small number of children would not tolerate all of the task and declined to finish them. This is described in the results section and discussed further below.

3.5.9.1 Raven's Standard Progressive Matrices (RSPM).

Raven's Standard Progressive Matrices (RSPM; Raven, Raven, & Court, 1998) is a widely used 60 item non-verbal test which measures two components of fluid intelligence: the capacity to think clearly and make sense of complex data (eductive ability); and the capacity to store and reproduce information (reproductive ability). The test contains five sections which require participants to identify a missing component in a series of figural patterns. The sections, which progressively increase in difficulty, require increasingly greater skill in encoding and analysing information. The RSPM is often used to assess children's non-verbal MA and is a necessary tool when examining children with neurodevelopmental conditions where CA is incongruent with MA. It has previously been used in children with Autism (e.g. Simard, Luck, Mottron, Zeffiro, & Soulières, 2015) and FASD (e.g. (P. Kodituwakku et al., 2006). In a sample of 6,529 children, Abdel Khalek et al (2005) reported that the RSPM has internal consistency (0.88-0.93 Cronbach Alpha) and good factorial validity (0.73-0.89) (Abdel-Khalek, 2005). The task was conducted according to the RSPM Manual (Ravens et al., 1998) with no time limit

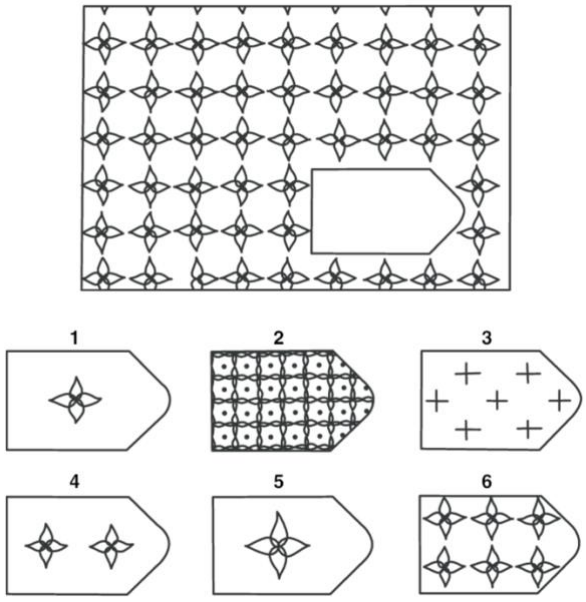


Figure 3.1: A sample question from the RSPM

3.5.9.2 British Picture Vocabulary Scale 3 (BPVS).

The BPVS was used in order to examine children's receptive vocabulary and calculate verbal MA. This task has previously been used in Autism (Hannant, 2018) and FASD (Brown, 2013) populations, both as a measure of MA and as a measure of receptive vocabulary. It consists of 168 words, divided into 14 sets which increase with difficulty. Each set contains twelve words which are read out to the child and shown alongside a picture. The child is required to point out the picture which corresponds to the word. Children's vocabulary ages are calculated from raw scores (ceiling item minus error), which correspond to standardised scores, and percentile ranks. From this, the child's vocabulary age can be calculated. In a sample of 3278, Dunn, Dunn, Style & Sewell (2009) reported that the BPVS had criterion validity with the Schonell Vocabulary Test of 0.8, and construct validity of 0.71 (Dunn et al., 2009). The task was conducted according to the BPVS Manual (Dunn et al., 2009) with no time limit.

Figure 3.2: BPVS test word 'Feline'

3.5.9.3 Digit span test of working memory

This is a task taken from the Weschler Memory Scale (Wechsler, 1997), and can provide a measure of short-term memory span, previously used in Autism (Barendse et al., 2013) and FASD (Crocker, Riley, & Mattson, 2015). The task involves reading digits aloud, after which the participant is required to immediately recall the sequence of digits. A sequence of two digits is read, then three, then four, and so on until a sequence of nine digits. The participant's Digit Span is the longest number of sequential digits that can accurately be recalled immediately. Participants are required to recall digits both forwards and backwards. In a sample of 55 children Sung (2011) reported high test-retest reliability of the digit span test (0.86). In a larger sample of 2,200 children, Canivez (2019) conducted exploratory and confirmatory factor analysis on the full Weschler Intelligence Scale for Children (WISC), finding that the coefficient for general intelligence was high (0.89) and the coefficients for group factors (including working memory) were lower, ranging from 0.87- 0.54 (Canivez, Watkins, & Dombrowski, 2017). The task was conducted according to the WISC Manual (Weshler, 1997) with no time limit.

3.5.9.4 Choice reaction time (CRT) continuous performance task

In order to assess children's sustained attention, vigilance, motor speed, inhibition and impulsivity, a choice reaction task (CRT) was designed in Matlab using a PsychTools authorised task (Matlab & Psychtools, 2020). A 2-choice task was used. This is similar to a simple reaction time task, however stimulus and response uncertainty are introduced by having two possible stimuli and two possible responses. This is in line with previous CRT tasks that have been used with children with FASD (Simmons, Wass, Thomas, & Riley, 2002) and Autism (Rinehart, Bradshaw, Moss, Brereton, & Tonge, 2001). The task was presented on a MacBook Air laptop with a 33cm screen and a viewing distance of around 50cm. The task required the child to respond to two different looking stimuli, a cartoon sloth, and a banana as can be seen in Figures 3.3 and 3.4

Figure 3.3: Sloth

Figure 3.4: Banana

When the sloth appeared on the screen, the child was required to press the 'left' arrow key. When the banana appeared on the screen, they were required to press the 'right' arrow key. Target stimuli appeared on the screen in a random sequence on a white background, with intervals of 0.5-2.00 seconds. Before the trial, it was ensured that the children were able to identify and discriminate between the objects, and relay the instructions, in order to ensure that the instructions were understood. Children were given verbal instructions: "*This is a sloth, and this is a banana. When you see the sloth, you must press this 'right' button. When you see the banana, you must press this' left' button*." In order to ensure the instructions were understood, further questions were asked: "*Which one is the sloth? When he comes up which button do you press? Which one is the banana? When it comes up which button do you press? Brilliant, shall we start?*" Correct answers elicited a positive 'bell' sound which is normally associated with correct answers, and incorrect answers elicited a negative 'buzz sound', which is normally associated with negative answers (Matlab & Psychtools 2020). When necessary, children were given positive feedback and encouraged to continue: "*well done, you're doing great! keep going"*. A practice trial, consisting of 10 targets, was administered. Five blocks of 20 trials were administered in the recorded reaction time. Outcome measures assess correct and incorrect responses, errors of commission and omission (late and early responses), and latency (response speed).

3.5.10 Statistical analysis

Data were analysed using the haven, glmnet and xtable packages in R, as well as IBM Statistical Package for Social Science V.22. Outlying scores were identified through Cook's distances and removed. Analyses where the significance of results changed once outliers were removed are labelled as 'OR' (Outliers Removed).

3.5.10.1 Group comparisons

Data were examined for normality using Levene's Test of homogeneity. To determine whether sex was a confounding factor, independent samples t-tests were used to compare males and females within the FASD and TD groups. Given the uneven ratio of boys to girls in the Autism group (17:4), where sex is used as a covariate hereon it does not refer to the Autism group. Regressions were used to investigate age-related changes in sleep, attention, fluid intelligence, working memory and receptive vocabulary. One-way ANOVAs were used to determine whether SES differences contributed to either sleep or psychological outcomes, per group. Since some age, SES and sex differences were found, all subsequent analyses were conducted using age, SES and sex as covariates.

Group comparisons between Autism, FASD and TD were made through one-way between-group Analysis of Variance (ANOVA), for each of the objectively defined variables: Sleep data (actigraphy), fluid intelligence/ nonverbal MA, receptive vocabulary/ verbal MA, working memory and attention. In post-hoc analysis where equal variances could not be assumed, the Games-Howell test was used. Where equal variances were assumed, the Bonferroni Correction was used, as set out in Field (2018).

3.5.10.2 Regression analysis

Regression analysis was conducted as per the methodology mentioned in the previous chapter, but with changes to collinear variables.

Hierarchical multiple linear regression using the Enter model was used to assess whether sleep was able to predict attention, fluid intelligence, working memory or receptive vocabulary, in Autism, FASD or TD groups. Block one always controlled for age, SES and sex. Tolerance statistics were conducted to examine the collinearity between variables. Actigraphy data was entered into Block two. Because there were several highly collinear actigraphy variables (>0.9), separate analyses were conducted for each actigraphy variable (bed time, wake time, assumed sleep time, actual sleep time, sleep efficiency, sleep latency, mean sleep bouts, number of night wakings, mean night waking duration, mean activity epoch, fragmentation). These variables were analysed separately in order to avoid Type II error, where results may be unreliable given high levels of collinearity.

Adjusted R^2 values are reported as the percentage of variance, in order to control for the number of predictors in the model.

ANCOVA interaction models were used to assess whether the strength of association between sleep and attention, fluid intelligence, working memory and receptive vocabulary was significantly different between groups.

Two-One-Sided Tests were conducted in R to assess for significant similarities between groups.

3.6 Results

The results from this study are laid out as follows: firstly, sleep data is described in order to give an overview of the quality and quantity of children's sleep. Secondly, children's performance on the experimental tasks is described, following the results of the relationship between the experimental tasks and sleep.

3.6.1 Sleep measures

3.6.1.1 Actigraphy

All children were required to wear an actiwatch for seven consecutive days and nights, however some declined to wear it for the full seven nights. Three children from the FASD group did not tolerate the watch and declined to wear it at all, and three children did not tolerate the watch for the full seven days. Three children from the Autism group did not tolerate the watch at all whilst one participant lost a watch. All TD children completed at least five school nights of actigraphy (across all three groups mean number of nights = 5.45). The final number of participants who completed a minimum of four nights of actigraphy was Autism (n=17), FASD (n=26), TD (n=45).

3.6.1.1.1 Group comparison

The actigraphy variables set out below were chosen to give a broad overview of sleep characteristics across the three groups. Group comparisons were made using ANOVA and Tests of Similarity. Group differences and similarities are outlined in Table 3.3, Figures 3.5-3.7, and reviewed in detail in the following discussion section.

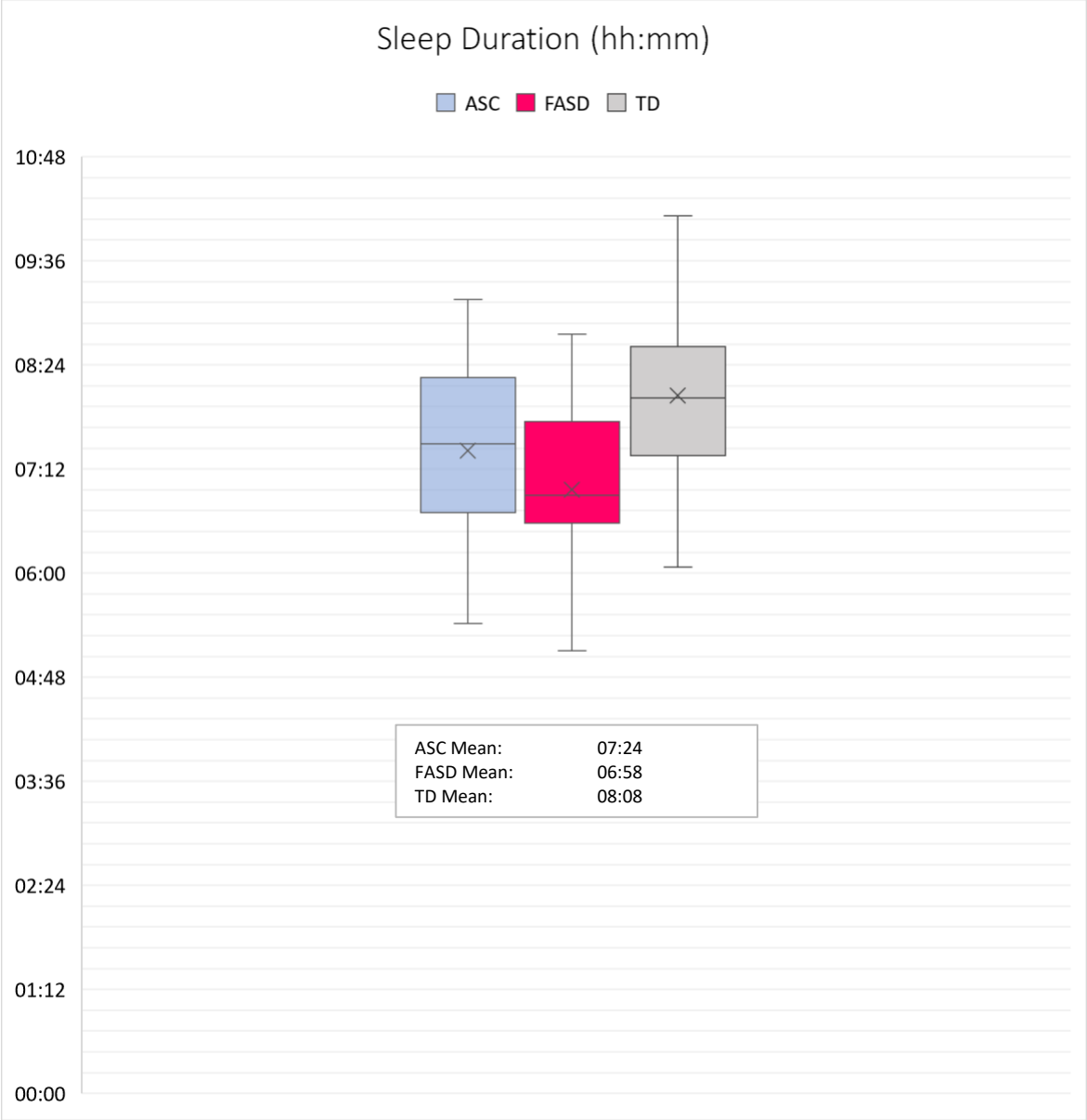


Figure 3.5: Sleep Duration (hh:mm): comparison between groups.

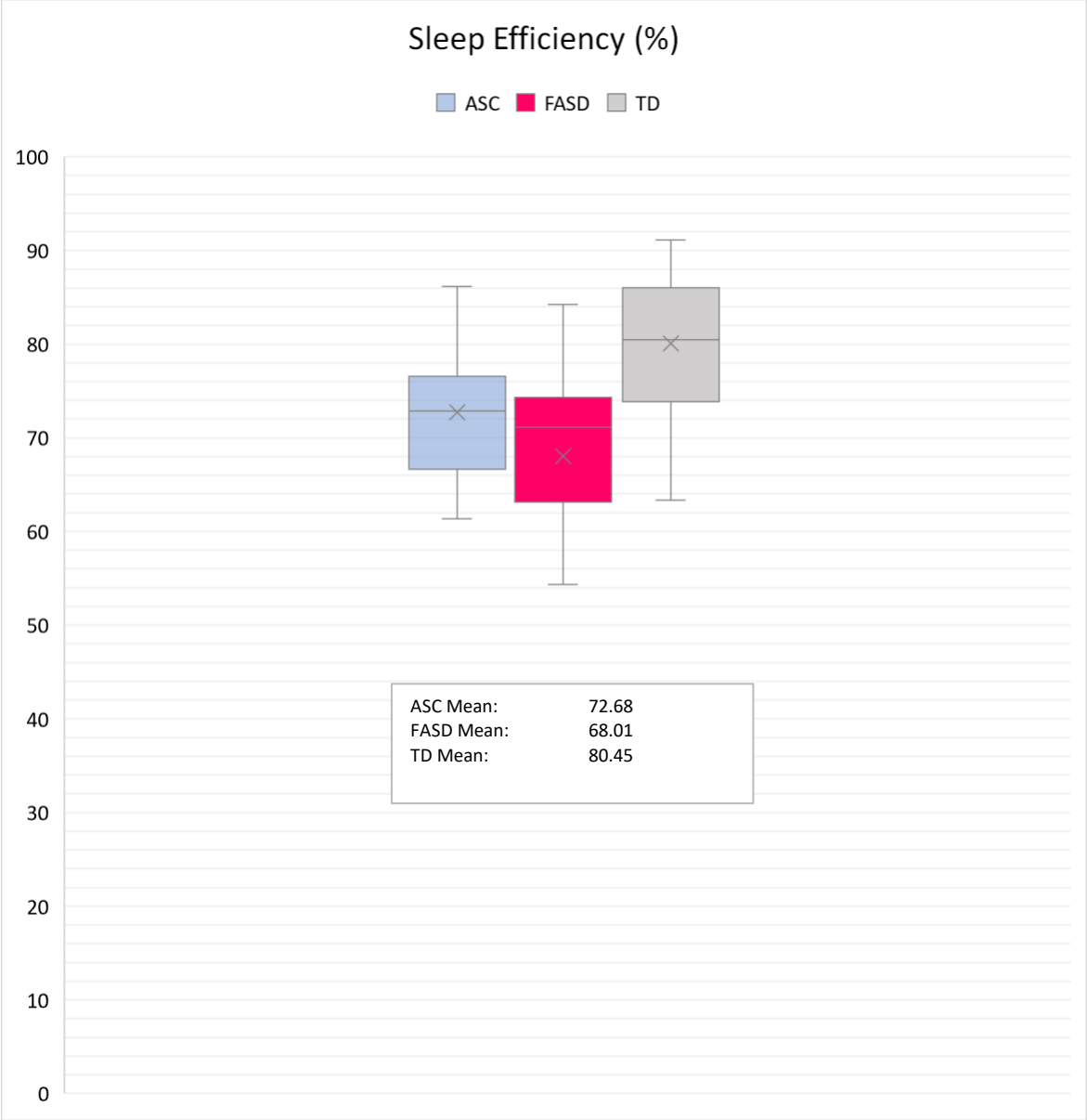


Figure 3.6: Sleep Efficiency as a percentage: comparison between groups

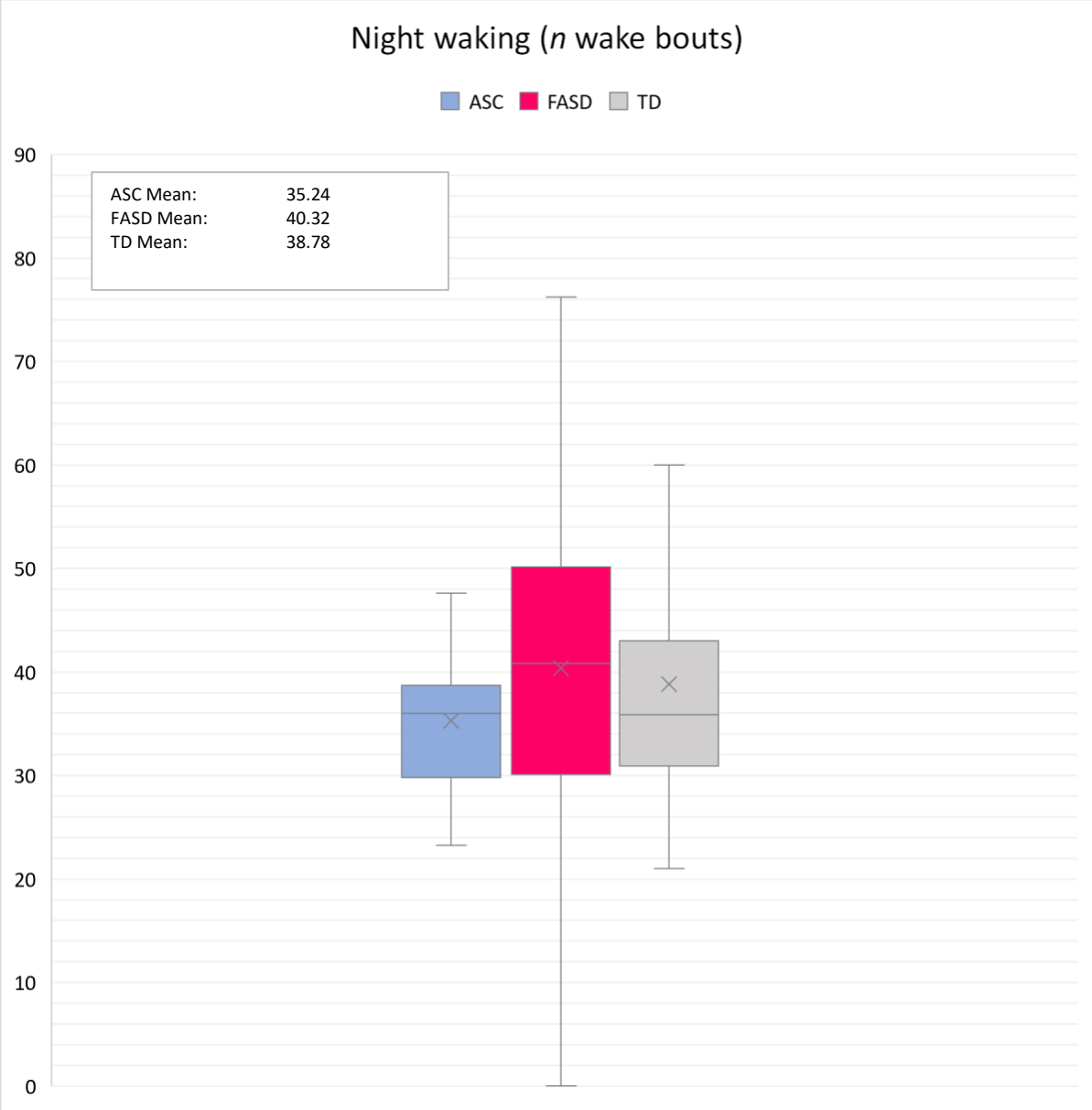


Figure 3.7: Mean Night Wakings (n): comparison between groups

Table 3.3: Mean scores and group differences using ANOVA for selected actigraphy variables

	Autism (*n*=17)		**FASD (*n*=26)**		**TD (*n*=45)**				
	Mean	SD.	Mean	SD.	Mean	SD.	F	*p*	np2
Bed Time	21:18:45	0:57:26	21:14:50	1:21:32	21:08:13	0:55:32	0.28	0.75[1]	0.01
Wake Time	0:07:03	0:01:13	0:07:06	0:01:10	0:06:59	0:00:43	0.13	0.88[1]	0.00
Assumed Sleep Time	9:12:52	1:00:52	9:29:20	0:57:11	9:45:58	1:18:25	1.42	0.25[1]	0.03
Actual Sleep Time	7:24:33	1:03:03	6:58:41	1:11:07	8:06:55	1:04:44	8.74	**<0.001**[2,3,4]	0.18
Sleep Efficiency	72.68	7.55	68.00	10.82	80.02	6.99	16.39	**<0.001**[2,3,4]	0.29
Sleep Latency	0:38:18	0:34:12	0:24:30	0:20:20	0:26:08	0:26:49	1.53	0.22	0.04
Mean Sleep Bouts	0:24:21	0:33:54	0:11:00	0:03:21	0:13:50	0:04:07	4.10	**0.02**[2,3]	0.14
Night Wakings (*n*)	35.24	7.20	40.32	16.73	38.61	13.65	0.67	0.51	0.02
Mean Night Waking	0:03:07	0:00:46	0:04:18	0:03:31	0:02:36	0:01:03	4.99	**0.01**[2,3]	0.11
Fragmentation Index	31.06	7.60	40.44	17.08	36.01	9.76	2.96	**0.05**[2,3,4]	0.07

[1]Significant Similarity between Autism and FASD (p=<0.05); [2]Significant Difference between Autism and TD (p=<0.05); [3]Significant Difference between FASD and TD (p=<0.05);
[4]Significant Difference between Autism and FASD (p=<0.05)

3.6.1.2 Chronological age and sleep parameters

Linear regression was used to assess whether there were any developmentally related associations between sleep and chronological age (CA). It was predicted that sleep parameters would change in accordance to age in TD, but not clinical populations. In summary, bedtime, wake time and mean sleep bouts were significantly correlated with CA however no significant trajectories were found in other actigraphy parameters. These are explained in more detail below.

3.6.1.3 Bedtime

Bedtime was significantly related to CA in the TD group with older children going to bed later. It was not significantly related to CA in the Autism or FASD groups (Autism: R^2= 0.09, $F_{(1,17)}$ = 1.43, p=0.25; FASD: R^2= 0.02, $F_{(1,25)}$ =0.45, p=0.51; TD: R^2= 0.10, $F_{(1,39)}$ = 3.39, p=0.05).

3.6.1.4 Wake time

Wake time significantly changed with age for children with TD children and those with Autism. Older TD children woke up significantly later, but older children with Autism woke up significantly earlier, regardless of the day of the week. There were no age related changes in the FASD group (Autism: R^2= 0.22, $F_{(1,15)}$ = 3.92, p=0.03; FASD: R^2= 0.003, $F_{(1,25)}$ = 0.6, p=0.78; TD: R^2= 0.11, $F_{(1.39)}$ = 3.5, p=0.04).

3.6.1.5 Mean sleep bouts

The mean number of sleep bouts (contiguous epochs of non-movement) increased significantly with age for children with Autism, but not for TD children or children with FASD (Autism: R^2= 0.15, $F_{(1,15)}$ = 3.66, p=0.04; FASD: R^2= 0.03, $F_{(1,24)}$ = 0.29, p=0.29; TD: R^2= 0.01, $F_{(1,39)}$ = 1.39, p=0.12).

3.6.1.6 Nonsignificant results

Some effect sizes were too small to state a significant result, but some β-values showed either small developmental trends, or no change with increased chronological age, both of which deserve to be mentioned here. Non-significant results can indicate whether there were no developmental changes and the variable stayed constant throughout childhood, whether there were slight trends but not significant enough to report, or no trend and no constant (Field 2019). These can be seen in Table 3.4.

Table 3.4: Non significant developmental trends.

	β	R^2	*p*
Assumed Sleep/ CA			
Autism	**0.26**	0.07	0.79
FASD	-0.15	0.02	0.10
TD	**0.00**	<0.01	0.72
Sleep Duration/ CA			
Autism	**-0.33**	0.11	0.14
FASD	-0.14	0.02	0.49
TD	**-0.02**	<0.01	0.91
Sleep Efficiency/ CA			
Autism	0.11	0.01	0.69
FASD	-0.16	0.03	0.43
TD	**0.02**	<0.01	0.89
Sleep Latency/ CA			
Autism	**-0.22**	0.05	0.42
FASD	0.07	0.01	0.72
TD	**0.01**	<0.01	0.93
Fragmentation/ CA			
Autism	-0.07	0.01	0.79
FASD	**0.21**	0.04	0.31
TD	0.06	<0.01	0.72

Highlighted Results: *β value of >0.2 indicates a slight but not significant trend whilst <0.05 indicates a constant, or no developmental trend*

3.6.1.7 SES and sex differences

In the TD group, SES was significantly related to bedtime, with higher SES participants sleeping earlier (R^2= 0.11, $F_{(1,17)}$ = 4.60, *p*=0.038).

Sex differences were not examined in the Autism group due to uneven sizes, but in the FASD group, girls woke up significantly later than boys (male: *m*=06:17, SD= 1:18, female: *m*=07:22, SD=00:58; t(24)=-2.4, *p*=0.02). In the TD group, boys were significantly more mobile at night, with mean activity epochs significantly higher than girls (male: *m*=27.98, SD= 9.97, female: *m*=21.32, SD=10.87; t(39)=2.04, *p*=0.04).

3.6.2 Objective versus subjective reports

Pearson's product moment correlations were conducted in order to investigate whether subjective parental report and objective measurements of sleep were similar to each other, using analogous CSHQ and actigraphy variables. These similarities can be viewed in Table 3.5.

Table 3.5: Pearson's product moment correlations between parent report and actigraphy

	Autism (n=17)		FASD (n=24)		TD (n=45)	
	β	**p**	**β**	**p**	**β**	**p**
Sleep Duration/ Actual Sleep	0.14	0.61	-0.21	0.32	-0.18	0.27
Sleep Onset Delay/ Sleep Latency	0.32	0.23	0.17	0.42	0.06	0.70
Night Waking / Wake Bouts	-0.42	0.11	-0.12	0.59	0.32	**0.04**
Total CSHQ / Actual Sleep	0.19	0.48	-0.15	0.50	-0.32	**0.04**
Total CSHQ / Sleep Efficiency	-0.21	0.43	-0.03	0.88	-0.31	**0.05**

3.6.3 RSPM/ nonverbal MA

The RSPM was used as a measure of nonverbal MA. Differences between the Autism, FASD and TD groups were investigated using one way between group ANOVAs, with Games-Howell post hoc comparisons. Associations between sleep and MA were investigated using hierarchical multiple regression, accounting for sex in the FASD and TD group, and SES in all three groups.

Nonverbal MA is calculated using the RSPM total score, out of a possible 36. Two children (one with Autism, one FASD) scored below the threshold of 5; Nonverbal MA was therefore calculated from the RSPM total score, as described by Ashworth (2013).

It was not possible to collect RSPM data from all participants. In the TD group, all participants completed the task, however in the clinical groups if a child became irritable or restless with the task, a break was given, and they were encouraged to return. Five children with FASD did not want to finish the task: two out of externalised aggression (e.g. picking the book up, throwing it on the floor) and three out of internalised fear (e.g. crying and going to a caregiver for comfort). One child with Autism

did not complete the task, due to peripheral and sensory overload (the child was preoccupied with thoughts, had impulsive behaviour and was unable to attend to the task).

3.6.3.1 Group comparisons between nonverbal MA

There were significant differences between Autism, FASD and TD groups in the RSPM total scores, indicating that nonverbal MA is distinct to each clinical profile and significantly different to TD populations (see Table 3.6). There were no significant associations between nonverbal MA, SES and sex.

Table 3.6: Between Groups one-way ANOVA for RSPM

	Autism (n=20)	**FASD (n=24)**	**TD (n=45)**	**f**	**sig**	**Autism/TD**	**FASD/TD**	**Autism/FASD**
RSPM Score *(M[SD])*	22.38 (8.81)	18.75 (10.01)	26.82 (6.83)	2.09	0.04	0.04	0.001	0.003

3.6.3.2 The relationship between CA and nonverbal MA

Significant linear regressions between CA and Nonverbal MA were found in all three groups (Autism: R^2= 0.22, $F_{(1,19)}$ = 5.26, p=0.03. FASD: R^2= 0.50, $F_{(1,23)}$ = 22.15, p=<0.001. TD: R^2= 0.57 $F_{(1,44)}$ = 55.81, p=<0.001).

3.6.3.3 Nonverbal MA and sleep

Nonverbal MA was found to be a predictor of bedtime, sleep efficiency, sleep latency, wake time, mean night waking and mean mobile activity in the FASD group, but not in the ASD group. Nonverbal MA was associated with later bedtimes in the TD group. Higher MA scores were associated with more sleep problems and lower sleep efficiency in the FASD group, however this was not the case in the TD or Autism groups. To give an overview of the associations between sleep and MA in FASD, results are shown in Table 3.11.

3.6.4 BPVS/ verbal MA

The BPVS was used as a measure of verbal MA. Differences between the Autism, FASD and TD groups were investigated using one way between group ANOVAs, with Games-Howell post hoc comparisons. Associations between sleep and MA were investigated using hierarchical multiple regression, accounting for sex in the FASD and TD group, and SES in all three groups.

Raw scores on the BPVS are calculated by subtracting the total number of errors from the ceiling item score. These raw scores are plotted against age norms which in turn identifies a child's verbal MA. However, because of the significant differences in age of the participants (the TD participants are on average younger than the FASD), it is more accurate to use standardised scores to account for the age differences.

All TD and Autism participants completed the BPVS task. Four children with FASD did not wish to complete the task.

3.6.4.1 Group comparisons between verbal MA.

Table 3.7: Between Groups one-way ANOVA

	Autism *n*=21	**FASD *n*=25**	**TD *n*=45**	***f***	***p***	**Autism/TD**	**FASD/TD**	**Autism/FASD**
BPVS Standard Score *(M[SD])*	95.09 (15.79)	87.16 (15.12)	98.91 (13.95)	5.136	0.008	0.79 *OR*	0.01 *OR*	0.05

There were significant differences between Autism/ FASD, and TD/FASD groups in the BPVS standard scores, however not a significant difference between Autism/TD (See Table 3.7). Children in the FASD group scored significantly lower than the other two groups each time. There were no significant associations between verbal MA and sex in the FASD and TD group. There were significant associations between verbal MA and SES in the Autism and TD group, but not the FASD group, with higher SES groups performing better on the receptive vocabulary task (Autism: ß = 0.39; *p*= 0.05. FASD: ß = 0.23; *p*= 0.07. TD: ß = 0.33; *p*=0.041).

3.6.4.2 The relationship between CA and verbal MA

Significant linear regressions between CA and verbal MA were found in the clinical but not TD group, with higher CA associated with higher verbal MA (Autism: R^2= 0.21, $F_{(1,20)}$ = 5.21, p=0.03. FASD: R^2= 0.46, $F_{(1,24)}$ = 19.24, p=<0.001. TD: R^2= 0.04 $F_{(1,44)}$ = 1.64, p=0.21).

3.6.4.3 Verbal MA vs sleep

Similar to nonverbal MA, children with FASD who were more cognisant experienced more sleep problems. Nonverbal MA was associated with later bedtimes in the FASD and TD group. A negative significant association was found between sleep efficiency and verbal MA in the FASD group. Further associations were found in mean mobile activity and sleep fragmentation in the FASD group. These associations are shown in Table 3.12.

3.6.5 Attention

A Choice Reaction Time task was completed by all TD and Autism participants. Seven FASD participants declined to take part in the attention task (six refused, one was overwhelmed by the number of activities that were being given).

Outcome measures were correct and incorrect responses (score out of 100), latency (response speed) and impulsivity (pressing at random).

3.6.5.1 Group comparisons between attention subsets

One- way ANOVA results showed that there were significant differences in correct responses, incorrect responses, reaction times and impulsivity. There were no significant differences or similarities between Autism/TD groups in Commissions, or Autism/FASD groups in omissions or impulsivity (see Table 3.8).

Table 3.8: Between Groups one-way ANOVA for CRT Task

	Autism (n=21) M [SD]	**FASD (n=22) M [SD]**	**TD (n=45) M [SD]**	***f***	***p***	**Autism/TD**	**FASD/TD**	**Autism/FASD**
Correct Responses	86.47(9.75)	85.41 (23.72)	93.8 (7.79)	3.56	**0.03**	0.12	**<0.001**	**0.05**
Reaction Time Correct	1162.17 (776.78)	942.27 (370.74)	862.86 (289.58)	2.93	**0.05**	**0.04**	**0.05**	**0.05**
Reaction Time Incorrect	799.67 (461.76)	2577.27 (8435.94)	683.61 (405.93)	3.56	**0.03**	**0.01**	**0.05**	**0.02**
Impulsivity	4.14 (6.69)	5.36 (21.23)	0.27 (1.27)	3.88	**0.01**	**0.03**	**0.04**	0.62

3.6.5.2 Developmentally related differences in attention

Chronological age was significantly related to reaction time in the TD, but not in the clinical groups. Older children had higher correct reaction times (Autism: R^2= 0.12, $F_{(1,20)}$ = 9.05, p=0.12. FASD: R^2= 0.08, $F_{(1,22)}$ = 2.67, p=0.19. TD: R^2= 0.31 $F_{(1,44)}$ = 10.67, p=<0.001).

3.6.5.3 Sex and SES differences in attention

There were significant sex differences in correct responses in the FASD group, with boys showing lower levels of vigilance than girls (male: M=78.92, SD=29.38, female: m=94.78, SD=3.99. t(20)=1.59, *p*=0.03)

There were no significant associations between attention variables and sex in the FASD and TD group. SES was not significantly related to attention variables in any of the groups.

3.6.5.4 Attention and sleep

Impulsivity and reaction times were associated with sleep fragmentation and sleep bouts. These results can be viewed in Tables 3.13 and 3.14.

3.6.6 Digit span test of working memory

The Digit Span test of Working Memory was completed by all Autism and TD children. Five FASD participants declined to take part for the same reasons listed in Section 3.5.3 above.

Outcome measures were noted as raw score forwards, and raw score backwards. Digit Span Age is calculated from age norms related to raw scores. Regression analysis used SES and chronological age as covariates in all three groups, and sex as a covariant in the FASD and TD groups.

3.6.6.1 Group comparisons for working memory

One- way ANOVA results showed that there were significant differences between digit span forward and backward raw scores, and significant differences in digit span age (see Table 3.9).

Chronological age was significantly related to forwards and backwards raw scores in the TD and FASD, but not Autism group, with older children tending to achieve higher results (Forwards: Autism: R^2= 0.24, $F_{(1,21)}$ = 5.99, p=0.02. FASD: R^2= 0.45, $F_{(1,23)}$ = 18.25, p=<0.001. TD: R^2= 0.26 $F_{(1,44)}$ = 15.36, p=<0.001; Backwards: Autism: R^2= 0.16, $F_{(1,20)}$ = 3.54, p=0.08. FASD: R^2= 0.33, $F_{(1,23)}$ = 10.29, p=0.03. TD: R^2= 0.45 $F_{(1,44)}$ = 34.54, p=<0.001).

Table 3.9: Between groups one-way ANOVA for Digit Span

	Autism (n=21)	**FASD (n=24)**	**TD (n=45)**	***f***	***p***	**Autism/ TD**	**FASD/ TD**	**Autism/ FASD**
Digit Span Forward (M [SD])	20.62 (7.02)	17.04 (6.33)	22.73 (5.30)	7.02	**0.001**	0.21	**0.001**	**0.03**
Digit Span Forward Age (M [SD])	120.33 (65.43)	87.75 (47.69)	140.49 (60.78)	6.31	**0.003**	0.44	**0.002**	0.15
Digit Span Backward (M [SD])	10.1 (5.30)	9.92 (4.37)	13.47 (5.86)	4.12	**0.019**	**0.05**	**0.02**	0.43
Digit Span Backward Age (M [SD])	94.67 (31.07)	96.67 (31.72)	112.62 (24.19)	4.12	**0.019**	**0.05**	**0.001**	**0.97**

3.6.6.2 Developmentally related differences in working memory

There were developmentally related differences relating to verbal and nonverbal MA. Overall developmentally related differences from both cognitive tasks of attention and memory in relation to verbal and nonverbal MA can be viewed in Table 3.10.

Table 3.10: Developmental related differences in attention and working memory

	Autism			FASD			TD		
	f	***p***	**r^2**	***f***	***p***	**r^2**	***f***	***p***	**r^2**
Verbal MA									
Reaction Time Correct	6.52	**0.002**	0.26	0.27	0.61	0.01	2.60	0.14	0.06
Impulsivity	2.73	2.12	0.13	3.49	0.77	0.15	10.78	**0.002**	0.20
Digit Forward Raw Score	5.07	**0.04**	0.21	33.61	**<0.001**	0.60	4.44	**0.04**	0.09
Digit Backward Raw Score	1.33	0.26	0.07	19.90	**<0.001**	0.48	0.00	0.99	0.00
Nonverbal MA									
Attention Correct (n)	1.82	0.19	0.08	6.38	**0.02**	0.25	3.63	0.06	0.08
Reaction Time Correct	8.22	**0.01**	0.30	0.39	0.54	0.02	2.33	0.13	0.05
Impulsivity	1.59	0.22	0.08	10.54	**<0.001**	0.36	0.01	0.93	0.00
Digit Forward Raw Score	7.74	**0.01**	0.29	44.06	**<0.001**	0.67	11.45	**0.002**	0.21
Digit Backward Raw Score	2.78	0.11	0.13	36.66	**<0.001**	0.63	19.12	**<0.001**	0.31

3.6.6.3 Sex and SES differences in working memory

SES and sex were not associated with digit span results in any of the groups.

3.6.6.4 Working memory and sleep

Working memory was associated with bedtime and sleep duration. These results can be viewed in Tables 3.15 and 3.16.

Table 3.11: Nonverbal MA and Sleep

	Autism (*n*=20)					FASD (*n*=25)					TD (*n*=45)				
	B	**SEB**	**ß**	**R2**	***p***	**B**	**SEB**	**ß**	**R2**	***p***	**B**	**SEB**	**ß**	**R2**	***p***
Bedtime	<0.001	0.001	0.11	0.37	0.66	<0.001	<0.001	0.32	0.48	**0.01**	0.01	0	0.316	0.6	**0.01**
Sleep Efficiency	0.1	0.07	0.35	0.12	0.18	-0.14	0.06	-0.47	0.18	**0.02**	-0.06	0.1	-0.09	0.02	0.57
Wake time	0.09	16.53	0	<0.001	0.99	76.1	23.75	0.58	0.34	**0.004**	44.82	80.61	0.09	<0.001	0.59
Mean night waking	-0.29	4.94	-0.16	0.03	0.56	2.89	1.4	0.42	0.14	**0.05**	-0.15	0.95	-0.26	0.03	0.87
Mean mobile activity	0.01	0.09	0.02	<0.001	0.96	0.42	0.14	0.56	0.28	**0.01**	-0.07	0.16	-0.07	0.01	0.65

Table 3.12: Verbal MA and Sleep

	Autism (*n*=21)					FASD (*n*=24)					TD (*n*=45)				
	B	**SEB**	**ß**	**R^2**	***p***	**B**	**SEB**	**ß**	**R^2**	***p***	**B**	**SEB**	**ß**	**R^2**	***p***
Bedtime	<0.001	0.001	0.11	0.37	0.66	<0.001	<0.001	0.32	0.48	**0.01**	0.01	0	0.316	0.6	**0.01**
Sleep Efficiency	1.78	1.28	0.34	0.16	0.18	-2.06	0.86	-0.46	0.22	**0.03**	-0.43	0.35	-0.19	0.04	0.23
Mean mobile activity	-0.06	1.13	-0.14	0.01	0.96	1.05	0.31	0.59	0.36	**0.003**	-0.14	0.23	-0.1	0.09	0.55
Sleep Fragmentation	-1.59	1.26	-0.31	0.1	0.227	0.97	0.41	0.44	0.21	**0.03**	-0.5	0.26	-0.31	0.01	0.84

Table 3.13: Attention Reaction Time Correct and Sleep

	Autism (*n*=21)					FASD (*n*=22)					TD (*n*=45)				
	B	**SEB**	**ß**	**R^2**	***p***	**B**	**SEB**	**ß**	**R^2**	***p***	**B**	**SEB**	**ß**	**R^2**	***p***
Sleep Bouts	1.25	0.31	0.29	0.32	**0.04**	0.97	0.4	0.09	0.03	0.57	2.97	0.34	0.47	0.24	**0.002**

Table 3.14: Attention Impulsivity and Sleep

	Autism (*n*=21)					FASD (*n*=22)					TD (*n*=45)				
	B	**SEB**	**ß**	**R^2**	***p***	**B**	**SEB**	**ß**	**R^2**	***p***	**B**	**SEB**	**ß**	**R^2**	***p***
Sleep Fragmentation	0.85	0.026	0.39	0.31	**0.003**	1.23	1.11	0.06	0.01	0.32	2.32	1.24	0.12	0.14	0.34

Table 3.15: Digit Span Forwards (raw score) and Sleep (working memory and sleep)

	Autism (*n*=21)					FASD (*n*=24)					TD (*n*=45)				
	B	**SEB**	**ß**	**R^2**	***p***	**B**	**SEB**	**ß**	**R^2**	***p***	**B**	**SEB**	**ß**	**R^2**	***p***
Bedtime	1.78	0.01	0.33	0.24	**0.01**	0.02	0.001	0.19	0.09	0.21	1.68	0.01	0.41	0.32	**0.01**

Table 3.16: Digit Span Backwards (raw score) and Sleep (working memory and sleep)

	Autism (*n*=21)					FASD (*n*=24)					TD (*n*=45)				
	B	**SEB**	**ß**	**R^2**	***p***	**B**	**SEB**	**ß**	**R^2**	***p***	**B**	**SEB**	**ß**	**R^2**	***p***
Bedtime	1.68	0.12	0.42	0.21	0.22	2.36	0.21	0.54	0.29	**0.05**	1.7	0.02	0.38	0.26	**0.04**
Actual Sleep	1.35	0.15	0.39	0.24	**0.01**	2.55	1.01	0.03	0.42	0.23	0.01	0	0.01	0.05	0.57

3.7 Discussion

The primary aims of this study were to investigate sleep characteristics and their association with working memory and attention in healthy TD children and children with FASD or Autism. Additionally, this study intended to examine whether findings were syndrome specific or developmentally related. In meeting these aims this thesis was successful: sleep, attention, working memory, vocabulary and fluid intelligence were objectively measured in the three groups, with sample sizes reported here large enough to calculate significant regressions. It was predicted that sleep and cognitive characteristics would be syndrome specific, and that better sleep would be associated with higher cognitive ability. It was also predicted that the developmental effects of sleep and cognition in the TD group would be in line with previous studies, but due to disruptions in neurodevelopment this would not be the case in the Autism and FASD groups. The results reveal a number of expected, novel, and unexpected findings. This section contains a discussion on these findings, how they relate to the predictions made in Section 3.3, and where they sit within existing research. This is followed by a discussion of the limitations of this study, its potential implications and suggestions for future research.

3.7.1 Sleep

3.7.1.1 Actigraphy

In summary, actigraphy data were mostly, but not completely, consistent with previous reports of sleep problems in children with FASD and Autism (e.g. Díaz-Román et al., 2018; Wengel et al., 2011). TD children experienced fewer sleep problems than children with Autism and FASD. Sleep problems showed a developmental trend in CA in TD but not in the clinical groups, and developmental trends in MA in the FASD group. Sleep problems were syndrome specific.

3.7.1.1.1 Prediction 1a: Children with FASD and Autism will have lower sleep duration and sleep efficiency, and higher sleep fragmentation than TD children (Díaz-Román et al., 2018; Inkelis & Thomas, 2018).

The present study partially supports the prediction made in hypothesis 1a, stating that sleep would be more disrupted and problematic in the clinical groups than the TD group. Previous studies measuring actigraphy parameters suggest higher levels of sleep disruption in Autism and FASD populations than TD populations, although these data are not generalisable and meta-analytical data suggest within-group heterogeneity (e.g. Chen et al., 2012; Díaz-Román et al., 2018). Nonetheless, sleep duration, sleep efficiency and sleep fragmentation scores were significantly different in all three groups, with lower sleep duration and efficiency and higher fragmentation in the clinical groups than TD group. There was evidence that these sleep parameters are syndrome specific given the significant differences between Autism and FASD samples in sleep duration, sleep efficiency and sleep fragmentation. Children with FASD slept for an average of 6 hours and 58 minutes, with an average of 68% sleep efficiency and 40% fragmentation. Children with Autism slept for an average of 7 hours and 24 minutes, with an average of 72% sleep efficiency and 36% fragmentation, whilst TD children slept for an average of 8 hours and 6 minutes, with an average of 80% sleep efficiency and 31% fragmentation. This specificity suggests that the neural mechanisms of sleep may mature and develop differently depending on the structural and functional differences that make up Autism and FASD.

To my knowledge, one other study has used actigraphy to measure sleep in children with FASD. Wengel and colleagues (2011) used actigraphy to measure sleep in 3 to 6 year-old children (*n*=19), but reported that sleep quality and duration did not differ between the FASD group and age matched controls. The inconsistency between the present study and Wengel et al. (2011) may be due to the differences in the age ranges of participants (3-6 years old in the Wengel et al. study, versus 6-12 years old in the present study), differences in sample sizes, and/or differences in the technology used. Children with FASD can reach age appropriate developmental milestones in the early years, but social,

emotional and cognitive development tends to delay at the start of school and plateau at around seven years old; hence the minimum age that a child can be referred to a FASD clinic being six years (Mukherjee, 2019). The present results suggest that, if 3-6 year old children do not experience significant sleep problems, but 6-12 year old children do, perhaps sleep also follows a similar developmental trend, plateauing at the same time as the cognitive domains. Additionally, Wengel et al. (2011) did not report numerical actigraphy results and the present study is therefore the first to report actigraphy variables for children with FASD, which further demonstrates the need for research in this field.

The present study findings are consistent with previous ones on sleep in children with Autism, however previous findings are not easily generalisable. A meta-analysis by Diaz-Roman and colleagues (2018) reported five studies that met their quality criteria for actigraphy findings in children with Autism. In this meta-analysis, children with Autism (*n*=140) slept on average 7 hours and 38 minutes, with an average of 73% sleep efficiency, whilst TD children (*n*=132) slept on average 8 hours, with an average of 90% sleep efficiency (Diaz-Roman et al., 2018). Sleep was also more fragmented in the Autism than TD group, and standard mean differences with 95% CI showed that children with Autism consistently presented with more sleep problems than TD children. However, within the same sample, sleep efficiency, sleep duration, fragmentation and assumed sleep was heterogenous which indicates a difficulty in generalising findings when using actigraphy results. Contrary to Prediction 1, and inconsistent with previous studies, sleep onset latency was not significantly higher in the Autism and FASD group than the TD group. There were also no significant differences in children's bedtimes, wake times and assumed sleep. This is discussed in more detail in the following two sections.

3.7.1.1.2 Prediction 1b: Sleep problems, as defined by sleep duration, efficiency and fragmentation, will be syndrome specific

The present study partially supports the prediction made in hypothesis 1b, stating that sleep problems will be syndrome specific. Sleep duration and quality, sleep bouts, night wakings and fragmentation were significantly different between the three groups, indicating that Autism, FASD, and TD groups had different sleep profiles. Meanwhile, tests of significant similarity revealed that bedtimes, wake times, and assumed sleep were significantly similar in the Autism and FASD groups. This means that even though children with Autism and FASD went to sleep at similar times, woke up at similar times, and caregivers thought they slept significantly similar amounts, children with FASD had poorer sleep than children with Autism within the time they were asleep. Naturally, this implies that sleep fragmentation should be higher in the FASD group than the Autism group. Possibly due to the high inter-individual variability of the present findings, the number and duration of night wakings did not differ statistically between the two clinical groups although non-significant results showed that children with FASD experienced more night wakings that lasted longer: children with FASD had on average 40 night wakings lasting around four minutes whilst children with Autism had on average 35, lasting around 3 minutes. Children with FASD had significantly increased fragmentation than both the Autism and FASD groups which may explain why, despite the fact that bedtimes and wake times were significantly similar between the two clinical groups, sleep efficiency and duration was significantly poorer in the FASD group.

Thus sleep efficiency, duration and fragmentation profiles of Autism, FASD and TD children appeared to be syndrome specific. The teratogenic effects of PAE result in neural structural and functional damage, affecting a thinner cortical structure and a loss of connectivity between cortical and subcortical layers. Autism Spectrum Condition is thought to be the behavioural result of overconnectivity in local regions (Fletcher-Watson & Happé, 2019). Consequently, the main neural differences between FASD and Autism are thought to be differences in global and local processing. Syndrome specificity regarding sleep therefore suggests that the cortical and subcortical maturation that is associated with NREM and some REM sleep (See Section 1.1.4.2) might develop differently in

Autism and FASD, but in an 'Autism' specific and 'FASD' specific way. Although it seems likely, without multiple replicated studies it is too early to tell whether syndrome specificity regarding sleep is definitely true between Autism and FASD and demonstrated the need for further studies in this field.

3.7.1.1.3 Results that were inconsistent to previous findings or contrary to predictions

Contrary to the prediction in hypotheses 1 and 2, sleep latency was not syndrome specific, nor was it significantly different between the three groups. Mean sleep latency for children in the Autism sample was 38 minutes which was 14 minutes longer than the FASD sample, and 12 minutes longer than the TD sample, although within all three groups there was high inter-individual variability. This is inconsistent with previous findings in actigraphy studies in children with Autism, where latency has tended to be significantly higher than TD populations and has shown the most homogeneity of variance (Diaz-Ramon et al., 2018). This inconsistency may be attributable to the lower sample size in this study than the ones mentioned in Diaz-Ramon's 2018 meta-analysis, but conversely, previous PSG reports measuring sleep onset latency are less clear (bearing in mind that sleep onset latency in a laboratory setting can yield inaccurate results, particularly in children with developmental conditions. Often sleep onset latency relies on sleep diary information which may also be inaccurate). In the same meta-analysis by Diaz-Ramon, sleep onset latency was heterogenous in this population when measured through PSG (p=0.32; n=211) and is less well known. Similarly, the study conducted by Wengel et al. (2011) found that sleep latency was the only actigraphy variable to differ significantly between the FASD and TD groups, whilst PSG findings are less clear. Of the two previous PSG studies on children with FASD, neither used a control sample and referent results were used as control comparisons (Goril et al., 2016; Chen et al., 2015). Nonetheless, there was high variability between the two results. Sleep Onset Latency in the PSG study conducted by Goril et al. (2016) was reported to be 32 minutes while in Chen et al. (2015) reported 15 minutes, although this inconsistency may be attributable to going to sleep in a new and strange environment. In the present study this inconsistency with previous actigraphy reports on sleep latency in Autism and FASD may be due to a

number of reasons. Firstly, there are various environmental factors that influence sleep onset latency, such as complex anxieties, problems with attachment and not understanding bedtime as a concept (Jan et al., 2010). Secondly, the average sleep latency for the TD group was 6 minutes higher than typical sleep latency in TD, which may have affected the significance of the comparative results.

3.7.1.1.4 Prediction 2: There will be age associated differences in cognition in children with Autism, FASD and TD children. It is expected that older children will perform better on cognitive tasks than younger children (Fletcher-Watson & Happé, 2019b; Novick Brown et al., 2012)

3.7.1.1.4.1 Chronological Age (CA) and Sleep

There were no significant CA related changes in sleep duration, sleep efficiency, sleep latency, night wakings or fragmentation in any of the groups although there were some non-significant trends which are discussed below. There were however CA related changes in bedtime, wake time and sleep bouts for some of the groups.

This cross-sectional study represents a period in child development in which the increasing volume of grey matter in the parietal and frontal lobes peak, before decreasing to give way to white matter, resulting in a decrease in delta power (Jenni & Carskadon, 2012). During this period, differences in sleep patterns emerge, such as increased daytime sleepiness, differences on school days and weekends, later bedtimes and wake times, and a mean reduction in overall sleep duration (Espie & Morin, 2012). It was therefore expected that sleep duration would decrease with CA. In general, there was a trend for shorter sleep duration with increasing CA, however effect sizes were too small for this to be a significant result. In the TD group, CA was related to later bedtimes and wake times as Espie & Morin (2012) report, with older children going to bed later and waking up later than younger children. This was not the case in the Autism group however, who woke up significantly earlier with increasing age, and experienced significantly more night wakings with increased CA. This was expected in the

Autism group given that longitudinal studies in this population report that sleep fragmentation increases with CA (Verhoeff et al., 2018).

3.7.1.1.4.2 Non-significant results in developmental trends

Although some effect sizes were too small to be significant, some smaller non-significant correlations attributable to chronological age and actigraphy variables emerged. In the Autism group, there was a small decrease in sleep duration, sleep latency and sleep fragmentation. In the FASD group, there was a small decrease in assumed sleep, sleep duration and sleep efficiency, an increase in fragmentation, and a slight increase in sleep latency. Non-significant β values close to zero may indicate that some variables remain at a constant rate during development (Field, 2018), however without the benefit of a longitudinal analysis this cannot fully be known. Nonetheless, in the TD group, scores remained mostly constant, decreasing slightly in sleep duration and increasing slightly in sleep fragmentation. This is supported by the body of literature maintaining sleep architecture changes throughout childhood (see Section 1.1.2). In the age range of the present study, sleep cycles tend to become longer, whilst SWS diminishes with a corresponding increase in stage II sleep (Espie & Morin, 2012). It is not possible to detect these changes using actigraphy but increases in fragmentation and night wakings together with shorter sleep duration can indicate lighter stages of sleep are emerging.

3.7.1.1.4.3 Verbal and nonverbal Mental Age (MA) and sleep

The present study measured MA through two measures, the BPVS, measuring the child's receptive vocabulary, and the RSPM, measuring the child's fluid intelligence. These two measurements were taken with the intention of forming a comprehensive look at the child's verbal and nonverbal MA. In the present study, nonverbal MA appeared to be syndrome specific however there were no differences between the TD and Autism group in verbal MA, when outliers were removed. The present study found that TD children had the highest mean MA, and the FASD group had the lowest, which was expected given the higher levels of learning difficulties in children with FASD (S. Lange et al.,

2017). Both clinical groups also tend to experience additional environmental pressures such as performance anxiety and cognitive exhaustion which can have an impact on cognitive scores. On a number of occasions whilst testing for this study it became apparent that the child was bored, not engaged or giving false answers, which will be discussed in the limitations section below. One way of identifying inaccuracies in results is to assess whether CA and MA are linearly related, and whether expected associations exist between MA and other scores. In all three groups MA and CA were linearly related however there were some interesting associations between MA and sleep in the FASD group. Children with FASD who were more cognisant experienced more sleep problems, which was an unexpected result. Perhaps this is due to the more cognisant children experiencing higher levels of anxiety and having a more sophisticated understanding of social and environmental stressors, which in turn contribute to sleep disturbances.

3.7.2 Cognitive Tasks: CRT and Digit Span

3.7.2.1 Prediction 3a: Children with Autism will score higher than children with FASD on the cognitive tasks; Prediction 3b: TD children will score higher than the clinical groups on the cognitive tasks. 3c: Children with FASD will present with higher levels of attentional problems, in particular inhibitory control (Mukherjee et al., 2013).

The present study used a computerised task to measure sustained attention and choice reaction time. It was predicted that children with FASD, a condition with high co-occurrence to ADHD, would have longer reaction times, more incorrect answers and higher impulsivity than the other two groups. The present study only partially supports this prediction. In comparison to TD children, children with FASD had fewer correct responses, higher impulsivity and took longer to react to stimuli. Previous work on sustained attention in FASD (e.g. Kooistra et al., 2011) show that children with FASD tend to have higher levels of inattention and lower task performance than TD children. In comparison to children with Autism, children with FASD had fewer correct responses and were slower to react to the choice stimulus. In children with Autism, delays in choice reaction have been noted as the result of an intact

ability to execute a movement but delayed ability to prepare for it (e.g. Rinehart et al., 2001) which can account for the non-significant results between the TD and Autism groups in correct and incorrect responses, but the difference in results for reaction times. Others however, such as Ferraro (2016), claim that reaction time and sustained attention in Autism populations is more heterogenous, and interpretation of attentional task results in this population should be made with care. Atypical attentional characteristics are well documented in Autism and form part of early indicators that lead to diagnostic referrals (Fletcher-Watson & Happé, 2019), but localised attentional *superior* abilities in Autism (such as the ability to focus on one task for longer periods than neurotypical individuals) demonstrate that sustained attention and vigilance, when directed towards a topic or task that is of interest to the individual, is not deficient . Similar attentional superior abilities also exist in the FASD population. Children with FASD can tend to focus on one particular subject, task or object for prolonged periods of time, such as playing with one object or pacing and running from one room to another repetitively without understanding the appropriate time to stop to take a break, including to sleep or eat. These are likely to be labelled as RRBI's, or strange or obsessional behaviours in FASD, but are now emerging as superior abilities in Autism (Brown & Mather, 2016). One limitation of this methodology therefore is that computerised tasks are not accurate at showing the true capacity of sustained attention in these populations because they do not appeal to a child's particular interest and show special or superior attentional ability. This is discussed further in the limitations section below and is an important area of further research.

The present study used a digit span test to measure working memory in the three groups. Due to cortical damage as a result of PAE, working memory, short term memory and memory consolidation problems are among the main cognitive issues in children with FASD (Lange et al., 2017). Given that tests of working memory in the Autism population are more heterogeneous (Habib et al., 2019), relying on visuospatial, phonological, attentional and executive control domains (Baddeley & Hitch, 1974; Limoges et al., 2013), it was therefore expected that children with FASD would score significantly

lower than the TD and Autism groups in the test of working memory. Interestingly, whilst the present findings established working memory differences between the clinical and TD groups, significant similarities emerged between the Autism and FASD groups on logarithmic digit span-backward scores. If this is examined within the working memory model of Baddeley and Hitch (1974; see Section 3.2.1), it suggests there might also be similarly impaired visuospatial, phonological, attentional and executive control functions in the two conditions. However, in the present study, sustained attention was found to be significantly different between the two groups, and in the previous study (Section 2.8.4), parentally reported executive function appeared to be syndrome specific. It may be the case that methodological issues in the present study have not offered a full or substantial picture of the working memory model, but if replicated studies arrive at similar results perhaps the working memory domain is arrived at using differently functioning attentional and executive control domains. It is beyond the scope of this thesis to make an argument for neuroconstructivism, but further studies in this field should assess PAE affected cortical and subcortical structural damage (evidenced in FASD), in comparison with overcompensated localised neural connectivity (evidenced in Autism). Both divergent neural pathways result in significantly similar 'impaired' domains, as well as advanced 'intact' ones such as the superior attentional abilities as mentioned above (Karmiloff-Smith, 2009).

3.7.2.2 Prediction 4: There will be developmentally related changes in cognitive tasks in all three groups (Happe & Fletcher Watson, 2019; Kodituwakku, 2009).

In general, children improved on all cognitive tasks with increasing CA. In comparison to the two clinical groups, TD children showed the strongest CA related improvements on the cognitive tasks. This was expected given the known differences in cognitive development between TD children and those with Autism or FASD (e.g. Bodner et al., 2014; Brown & Mather, 2016).

In the Autism group, verbal and nonverbal MA was related to correct reaction times and digit score forward, but not related to impulsivity or digit score backward. The FASD group saw the most MA

related cognitive results: verbal MA was related to digit scores forwards and backwards, but not to attention, while nonverbal MA was related to attention (correct hits), impulsivity, digit score forwards and backwards. In the TD group, verbal MA was related to impulsivity and digit score forwards, while nonverbal MA was related to digit scores forwards and backwards. Standard Deviation scores indicate higher levels of variability in the Autism cognitive and MA scores, which may be a reason for this outcome. Overall, in all three groups, MA was associated with both cognitive tasks, which as predicted suggests that brain maturation is related to higher order cognitive skills across the three groups.

3.7.2.3 Prediction 5: Sleep and cognition will be linearly related in Autism, FASD and TD groups. The higher the sleep duration and sleep efficiency, the higher the cognitive ability (Inkelis & Thomas, 2018).

Multiple regression analyses were performed to examine whether sleep parameters assessing sleep duration, sleep quality, sleep efficiency and sleep fragmentation were predictors of working memory and attention in the three groups. It was predicted that, after controlling for CA, sex and SES, children with better sleep quality and duration would perform better in the cognitive tasks. The models demonstrated that a number of sleep parameters predicted cognitive outcomes in the Autism, FASD and TD groups, but that some results were inconsistent with the hypothesis.

In the Autism group, sleep duration predicted 24% of the variance in working memory scores and 31% of the variance in impulsivity. Longer sleep duration was associated with shorter correct reaction times in the CRT. In the FASD group, later bedtimes predicted 29% of the variance in working memory scores, whilst in the TD group, sleep parameters predicted 26-32% of the variance in working memory and 24% of the variance in correct reaction times. In summary, sleep was a significant predictor of working memory and attention in the Autism and TD groups, but not in the FASD group.

In the present study, TD children who experienced higher sleep efficiency had longer digit spans. This is consistent with previous work on the relationship between sleep and working memory in

neurotypical individuals, where sleep disruption is associated with reduced performance in working memory tasks (Espie & Morin, 2012). This performance decline is mediated by neural connectivity in the frontal and parietal areas (Chee & Choo, 2004). Since working memory is an important part of cognitive performance, reduced ability in this domain implies reduced task performance in several neurocognitive domains.

The present study found that children with Autism who slept longer had longer digit spans. This is consistent with hypothesis 7 and is supported by previous work by Calhoun and colleagues (2019) where, in a sample of adolescents with Autism (*n*=96), digit span tests and actigraphy revealed that working memory was linearly related to sleep disturbances. In the FASD sample however, the only sleep parameter to be associated with working memory was bedtime: the later the child's bedtime, the longer the digit span. One obvious reason for this is that older children had later bedtimes and so longer digit spans were related more to the developmental trajectory, despite CA being controlled for in the model. Other than bedtime, neither working memory nor attention appeared to be significantly associated with sleep in the FASD group (although nonsignificant results with smaller effect sizes did show associations between sleep and cognition). This is inconsistent with hypothesis 7 which predicted that cognitive outcomes would be predicted by sleep in the FASD group. It is unclear why these relationships are inconsistent between the groups, but one reason may be due to the underlying structural damage to the prefrontal areas caused by PAE. Astley and colleagues (2009) conducted fMRI assessments on a sample (*n*=58) of children with FASD, whilst administering the *N*-back working memory task, in which amongst a series of faces that were presented, participants were required to identify duplicate consecutive and non-consecutive images. Performance was poorer in the FASD sample than control sample, and performance on the task was marked by significant deficits in long-range prefrontal, posterior and parietal lobe function (Astley et al. 2009). Hence, working memory problems are intrinsic to the FASD neurocognitive profile due to this functional deficit (Lange et al., 2017). Meanwhile, in TD populations, prefrontal and parietal areas continue to mature into

adolescence, and are thought to have an association with sleep since this later maturation makes these areas vulnerable to the effects of sleep disruption (Beebe, 2011). Firstly, as outlined in Section 1.1.4, one of the functional processes of SWS is the consolidation of memory through global cortical and subcortical areas. During this time, prefrontal areas appear to 'functionally disconnect' from other regions (Beebe, 2011). Secondly, after sleep deprivation has occurred, prefrontal areas are less able to attend to cognitively demanding tasks, and theta waves can be observed which correspond with diminished working memory function and sustained attention (Carskadon & Dement, 2011). As Beebe (2011) suggests, cognitive deficits can be created through sleep deprivation and chronic sleep disruption. It may be the case that in FASD, global structural and functional damage due to PAE has caused working memory deficits, which, since they are intrinsic to FASD, will not be associated with sleep to a significant extent. It is unclear whether this association would improve with sleep intervention but this result demonstrates the need for this area of research.

3.7.2.4 Prediction 6: Caregiver reports on sleep will be inconsistent with objective measurements (Espie & Morin, 2012).

It was predicted that parent report would be inconsistent with objective sleep measurements. Although there were some similarities in all three groups, only the TD group passed the threshold of significant correlations between CSHQ and actigraphy variables. Night Waking as measured on the CSHQ were significantly related to Wake Bouts as measured through actigraphy in the TD group. Additionally, Actual Sleep and Sleep Efficiency were negatively correlated with CSHQ total in all three groups, but only significant in the TD group. This is consistent with previous studies. In a PSG, actigraphy and CSHQ validation study conducted by Markovich et al. (2015) on a sample of TD children (*n*=30), the only CSHQ and actigraphy variable that was analogous was Night Waking (Markovich et al., 2015). Additionally, caregivers were not accurate at reporting sleep duration across the three groups, which is consistent with the argument that there are inaccuracies in subjective caregiver reports, and such studies should be supported with objective studies.

3.7.2.5 Prediction 7a: Sex will be associated with cognitive outcomes in all three groups. It is expected that girls will score higher than boys in cognitive measures (Corcoran et al., 2011). 7b: SES will be associated with cognitive outcomes in all three groups. It is expected that those from higher SES will score higher than lower SES in cognitive measures (Corcoran, Crusius, & Mussweiler, 2011). 7c: SES will be associated with sleep disturbances in all three groups. It is expected that those from lower SES will have lower sleep duration and higher sleep fragmentation than higher SES (Corcoran, Crusius, & Mussweiler, 2011)

In the TD group, SES was a significant predictor of bedtime, with those from higher SES backgrounds sleeping earlier. Children with Autism and TD children from higher SES backgrounds performed better on the receptive vocabulary task than those from lower SES backgrounds. It was predicted that SES would be a mediator in the FASD group given that around 80% of children born with FASD are born into situations of psychosocial risk, such as cyclical poverty or to a biological parent with a substance addiction (Price et al., 2017). Psychosocial risk factors can have an impact on daily behavioural, adaptive and cognitive functioning (Brown & Low, 2008), and factors such as chaotic home environments, overcrowding and noise have a negative impact on sleep and academic performance (Marco, Wolfson, Sparling, & Azuaje, 2011). Additionally, SES can have an impact on parent-child relationships and children's educational outcomes (Brown & Low, 2008). It would be expected therefore that children from higher SES backgrounds score higher in cognitive tasks, but perhaps this is not the case in the FASD group as the SES backgrounds have become more evenly distributed after children have been placed in foster care.

3.8 Limitations

A number of limitations to this study have been noted above. The present study, and many previous large-scale ones, have reported the diminished intellectual abilities of children with FASD through

measuring ability on standardised scales (e.g. Streissguth et al., 1996, Nash et al., 2009). These studies have noted that children with FASD consistently score lower on tests of cognitive ability but one limitation here is that cognitive exhaustion, performance anxiety and negative school experiences may cause children to withdraw from laboratory or classroom like settings. During the testing procedure in the present study, it became apparent that the FASD participants needed more support and encouragement from both the experimenter and caregiver than the Autism and TD children. Children with FASD tended to react negatively when confronted with an item of 'schoolwork' and almost all FASD participants refused to initially take part, particularly at the beginning of the set of tasks. Children would also become overwhelmed by tasks and were aware that their cognitive capacities were being tested. It became apparent that one child (aged 11) was deliberately giving the wrong answer every time, which was ascertained when the task was paused and a picture from the BPVS set 1 (age 3) was shown containing: 1. Pencil, 2. Cat, 3. Hairbrush, 4. Sock. The child was asked to name the items on the picture and named them 1. Cat, 2. Toothbrush, 3. Sock, 4. Balloon. The child's caregiver encouraged him to volunteer the correct answer, but it became apparent that this was an attempt at a refusal to take part. Conversely, other children tried to 'cheat' by moving from their chairs to look at the answers. One child was overwhelmed by the BPVS after he did not know an answer and was thereafter too preoccupied with having given the wrong answer to take part further. Whilst controlled settings and standardised tasks measure cognitive ability, they also require that the child is not experiencing overload; this is not only a priority for cognitive testing in FASD but should also offer an insight into how educational strategies can address children with FASD.

Similarly, in the task of sustained attention, both children with Autism and FASD may not have exhibited the full extent of their attentional capacities as the task was not of interest to them. As mentioned above, children with Autism and FASD can show advanced sustained attention when attending to particular games, videos or interactive activity, but may not show the same motivational attention when presented with a cognitive attention task. This may mean that the child obtains a low

score on a controlled attentional task but is actually capable of longer sustained attention. Conversely, a ceiling effect emerged within the attention task in the TD group, with 16 children (36%) making no errors.

In the working memory task, children with FASD developed a way to 'figure out' how to recall the backwards digit span, without using the backwards working memory construct. The number was read out (e.g. "1,3,5,2,7"). The child would then repeat the number quietly, but only emphasise the final number (e.g. "1,3,5,2...***7***",“1,3,5..***2***"). Although working memory and higher order cognition was used to satisfy the answer, backwards working memory was not employed in these instances. Where it was apparent that this was occurring, the task was restarted with repeated instructions, however it was only apparent that this was occurring when the children were quietly repeating the numbers forwards.

In the RSPM, some TD children were at an advantage if they had completed similar nonverbal puzzles or IQ tests before. Some children were seeing such a task for the first time and did not immediately know how to complete it. Instructions were given as per the RSPM manual, however, some children were more able to answer correctly if they had previously completed a similar task or puzzle. This is often a problem with the RSPM since nonverbal tasks are less frequently used in primary educational settings than when the normative data for standard RSPM scores were collected (between 1984 - 1987; Raven, Raven & Court, 2000)

One way of overcoming these limitations, albeit time consuming and expensive, would be to conduct in depth studies with children with FASD, as well as with their caregivers and teachers in order to build a wider picture of the child's abilities. Such studies ought to be complemented with in school or at home observations of children to see their cognitive capacities in a relaxed and normal environment.

Finally, whilst attempts were made to refrain from emphasising this as a sleep study, it was explicit that children's sleep would be measured. For this reason, there may be a sample bias within the

clinical groups as caregivers with children with sleep problems were more likely to take part (see Appendix for recruitment materials).

Chapter 4

4.1 Thesis Summary

This thesis presents the first two studies comparing sleep and daytime function in children with Autism and FASD. Whist there is a paucity of sleep data concerning the FASD population, the studies contained within this thesis contribute to the growing body of literature reporting sleep and its correlates in Autism. Sleep was found to be a predictor of cognitive domains, domains of affect, and adaptive behaviour in not only the two clinical samples but also TD. Sleep problems were also more likely to be at higher, clinical levels in the Autism and FASD groups than in the TD groups. Therefore, it is proposed here that sleep within these populations is of clinical concern, and that sleep assessments and interventions should be designed specifically for children with Autism and FASD, given the variability of their neurodevelopmental profiles as well as their apparent sensitivity to sleep disruption. It is also proposed here that within these two clinical populations there exists a complex interplay between sleep and several domains that are crucial during development. This thesis supports the claim that caregivers, clinicians and educators ought to be informed of both the importance of sleep to the neurodevelopmental process, and provided with strategies for addressing sleep behaviour and sleep hygiene.

In Study 1, measurements from three inter-related domains were taken: anxiety, behaviour, executive function. To recap Bowman (2018), behaviour is an expression of an emotional response, governed by executive control. Bowman uses the example of a car accident: if an individual is driving along a certain road and hits a car coming out of a junction, executive control mechanisms file the episodic memory alongside the fear emotion. The following instance the same junction is passed, the fear associated with this episodic memory resurfaces, and a maladaptive behaviour such as avoidance follows. This neuronal pathway was phylogenetically intended to protect humans from predators, to remember where predators were most likely to be encountered, and manifests in 'fight or flight' behaviour. Further strengthening these fear connections results in a pathological fear, which in turn

becomes the fear and worry associated with anxiety. Thus, behaviour is conceptualised as the result of constructed emotional and executive control responses. In examining the anxiety, behaviour and executive functioning profiles of clinical groups where these three domains are compromised, it was possible to begin an exploration into Bowman's Triad concept using the examples of Autism and FASD. However, it would not have been novel to measure these characteristics side by side, since (as outlined in Section 1.4) several cross-syndrome comparisons have compared the neuropsychological domains of Autism and FASD (albeit without using this particular battery of measurements). Adding the variable of sleep allowed for a cross syndrome regression comparison between the Bowman Triad and sleep, a known associate of anxiety, executive functioning and maladaptive behaviour.

Although there are caveats and cautions regarding apparent significance, the results of Study 1 revealed several significant regressions which may provide novel contribution to the study of sleep and neurodevelopment. When placed visually (see Section 2.9), it appeared that some significant regressions clustered around particular groups and variables, even when sex, age and SES were accounted for. In the TD group for example, almost every maladaptive behavioural subscale (withdrawn, somatic, anxious, social problems, thought problems, delinquency, aggression and composite score) was significantly correlated with daytime sleepiness. This was not the case in the Autism or FASD groups. Similarly, high levels of executive functioning problems were apparent in relation to sleep duration in the two clinical groups, but not the TD group. In the Autism group, fear-based anxieties were related to sleep anxiety, whilst in the FASD group executive functioning was more related to sleep anxiety. Because some significant regressions appear to cluster around sleep parameters across different syndromes, it is tempting to claim sleep may serve different domains depending on neurodevelopmental profile and environmental input. However, it must be noted that cross sectional data cannot give us causal information.

Syndrome specificity (defined as when ASC/FASD; FASD/TD; ASC/TD all yielded statistically significant differences) was found in some subscales of executive functioning (shifting, organisation of materials, monitoring and emotional control; Autism consistently scoring higher than FASD) and behaviour (delinquency; FASD scoring higher than Autism). Whilst there may be similarities in behaviour and affect in the two populations, several executive functioning domains appeared to have what is conceptualised here as syndrome specificity. If this can be generalised to the greater Autism and FASD populations, it may suggest phenotypic differences in executive control and rule following. This has important implications for caregivers and professionals working with children with FASD, where resources that are aimed at children with Autism are often reused for children with FASD (Catterick & Curran, 2014). If executive functioning profiles are variable then resources aimed at Autism may not be appropriate for the learning needs of a child with FASD. For example, the present results suggest shifting from one task to another is more difficult for a child with Autism than it is for a child with FASD, but rule following behaviour is more difficult for a child with FASD than a child with Autism. Interventions used in the classroom therefore, such as a timer to count down until the next activity to allow time for adequate 'shifting', may not resonate with a child with FASD where rule following behaviours (as seen in ODD and conduct disorder) are likely to interfere with concepts such as teacher-facilitated schemes of work/ timetables.

This thesis is a cross-syndrome comparison between Autism and FASD, however it makes a novel contribution to the field because it is not simply a comparison of the differences between the two clinical samples, or an assessment of which clinical thresholds are met: tests of *similarity* allow the researcher to assess whether two sets of data are statistically significantly similar. Previous literature examining Autism and FASD have assessed significant differences between the neurodevelopmental profiles, or assessed whether one clinical group fits the diagnostic criteria of the other (e.g. Bishop et al., 2007; Mukherjee et al., 2011). The present studies yielded similar results to previously conducted cross syndrome comparisons between Autism and FASD, but tests of similarity can add an extra

dimension to this. For example, the present results concur with Bishop et al., (2007) who found that both their Autism (*n*=33) and FASD (*n*=29) samples presented with social communication difficulties that were at a clinically significant level (as ascertained by ADI-R). In Study 1 (albeit not as rigorously or objectively as Bishop and colleagues), it was similarly found that both children with FASD and Autism reached clinical levels for social communication difficulties, as well as a number of other cognitive, behavioural and affect related clinical thresholds found throughout Study 1 and Study 2. Another cross-syndrome comparison was conducted by Mukherjee and colleagues (2011) and outlined in Section 1.4. In Mukherjee et al. (2011), children with FASD and Autism both displayed clinical levels of withdrawn behaviour. Study 1 similarly found that both FASD and Autism groups reached clinical thresholds for 'Withdrawn' as a CBCL subscale, but additionally found that there were statistical similarities between Autism and FASD in the subscale of 'Withdrawn'. This statistical similarity was not found in the subscale of social/ communication and therefore cannot (using the present results) be applied to the Bishop et al. (2007) results. Therefore, adding tests of similarity allows us to understand past whether the two sets of means simply reach a threshold, but also to what extent two neurodevelopmental profiles might parallel each other. Two-one-sided-tests revealed several statistically significant similarities between the Autism and FASD groups in behaviour (withdrawn behaviour), and anxiety (panic, separation anxiety, physical injury, generalised anxiety and SCAS total). This provides a novel methodological contribution and can be utilised in the future in order to further assess the FASD profile.

Study 2 examined two cognitive domains (working memory and attention) against sleep and CA/MA. As outlined in Section 3.7 There was high variability within the two clinical groups in the cognitive tasks, supporting the argument that both children with Autism and FASD can show typical and atypical cognitive functioning. Children with Autism and TD children showed minimal differences in verbal MA scores, digit span forward, and attention scores. Developmental effects were found across the three groups in cognitive scores. Few associations were found between sleep and cognition across the three

groups, and whilst sleep was associated with attention and working memory in the Autism and TD group, it was not in any meaningful way in the FASD group. Since this is the first study to report the association between sleep and cognition in FASD, it is not possible to compare this study with previous similar ones. In Autism research, previous meta-analyses assessing sleep and psychological domains reveal heterogeneity in results (e.g. Diaz-Roman et al., 2018), possibly because sleep and cognition also contain high inter-individual variability and future studies may require larger sample sizes and uniform methodology. Nonetheless, the present study is the first to report both Autism and FASD sleep data side by side, the first to do so for the FASD population and for that reason provides a unique contribution to the field of developmental psychology.

4.1.1 Limitations summary

As mentioned throughout the discussion sections of this thesis, several limitations to these studies are noted. Validation issues with the CSHQ mean that it is not the most reliable sleep measurement tool available for paediatric populations. It is not validated for neurodevelopmental populations, or for the upper range of the sample age in Study 1. This may have yielded some inaccurate significant results, which can be identified/ rectified through future replicated studies and a push for other sleep measurement instruments to be more widely used. Additionally, whilst it was noted that caregiver report may not support objective reports, the CSHQ was inconsistent with actigraphy. This may have been because of 'first night' or 'participating in a sleep study' effects (several caregivers commented on how the watch served as a visual reminder that sleep habits were being monitored, which they felt led to smoother bedtimes resulting in better sleep for the week of the actigraphy). There were additionally sample limitations. Care was taken to not include any children with diagnoses of both FASD and Autism and both the NST and CARS were used to assess overlapping symptoms. No child with FASD who scored at clinical levels on CARS participated in either study, however this cannot guarantee that children with FASD with *any* Autism characteristics were excluded. There may also

have been sample bias in this study which was at first advertised as a study assessing sleep in Autism and FASD.

Significant results were assessed within this thesis as those yielding effect size larger than 0.3, *p* value <0.05, and pre and post hoc power analyses to examine the extent to which it is likely the data translates to the population. Ensuring viability when assessing significant results is important to experimental and novel work and there are several limitations to these statistical measures. *P* values are a widely used measurement of significance in scientific literature, but have several disadvantages as they could indicate significance when there is none, or provide a simplistic and binary view of significance. It may be the case, as Ranstram (2012) suggests, that confidence intervals and other measurements of significance should be used alongside *p* values in order to assess significance. Similarly, a-priori power analyses are adept at measuring the number of participants that are needed to explore a phenomenon in the population, but post-hoc analyses are constrained in their ability to offer much more than the results already gained (Field, 2018).

It was also demonstrated here that differences between caregiver report and objective measurements should be taken into consideration for future studies assessing sleep in atypical populations. However, according to both caregiver report and objective measurements, getting to sleep and staying asleep appeared to be more problematic in the clinical groups than the TD group.

Additionally, the samples represented here are not necessarily representative of the wider population and further replicated studies, preferably with longitudinal, stratified samples would provide more of an indication of sleep and daytime characteristics in the wider population. Some statistical limitations are also of note: when multiple regressions are being analysed, there can sometimes be a tendency to overinterpret significant results within the sample to the whole population. The most this can be rectified is through F ratios to assess the degrees of freedom there are likely to be between the sample

and the population, or a-priori and post hoc power analyses which assess the likelihood of high applicability to the population based on sample size (Field, 2018). Meanwhile, power analyses are not efficient or reliable at generalising to the population (Faul, Erdfelder, Lang, & Buchner, 2007; Zhang et al., 2019)

4.1.2 Future studies

The most reliable way to ensure certain phenomena exist within the population is through replicated studies and meta-analyses. Future correlational studies in Autism and FASD can ensure the robustness of the claim that there is a relationship between daytime functioning and sleep in these clinical populations. In turn, it would be ideal to ascertain whether this correlational relationship is causal. Sleep intervention studies are much needed both in FASD as well as Autism, and are areas of immediate concern. Primarily this is because it is now established that sleep is crucial to healthy neurodevelopment. Future studies should also include further PSG and actigraphy data in the FASD population as there is a scarcity of data here aside from the present thesis and the two previously mentioned studies. This would enable researchers to gain an understanding of the sleep architecture in this population.

If attempting to extend work on behavioural profiles and sleep, future studies could replicate this study on samples of children with a diagnosis of FASD, diagnoses of FASD and ADHD, and pathognomonic ADHD. This would contribute some understanding of the relationship between PAE and attention. One methodological suggestion for future studies is further use of the two-one-sided test, which can assess significant similarity between two sets of means.

Sleep problems are a burden on caregivers, family and the children involved. Sleep intervention studies and correlative studies can contribute to the understanding of the function and impact of sleep

in Autism and FASD, with the ultimate aim of creating an impact that can alleviate some of the stresses and burdens faced by children with Autism and FASD, as well as their caregivers. There is a pressing need for resources on sleep hygiene or behavioural interventions specific to the sensory, perceptual, attentional specifics of children with either Autism or FASD. More importantly, there is a general lack of awareness of FASD amongst professionals who may not realise they are coming across a child with PAE (Brown & Mather, 2016). Although training and resources exist in social work and social care settings where the presence of FASD is more well-known (Catterick & Curran, 2014), resources and training for special educational needs co-ordinators (SENCOs), educational psychologists and teaching staff would be beneficial in extending the knowledge of this little known but impactful developmental condition.

References

Abdallah, M. W., Greaves-Lord, K., Grove, J., Nørgaard-Pedersen, B., Hougaard, D. M., & Mortensen, E. L. (2011). Psychiatric comorbidities in autism spectrum disorders: Findings from a Danish Historic Birth Cohort. *European Child and Adolescent Psychiatry*. https://doi.org/10.1007/s00787-011-0220-2

Abdel-Khalek, A. M. (2005). Reliability and factorial validity of the standard progressive matrices among Kuwaiti children ages 8 to 15 years. *Perceptual and Motor Skills*. https://doi.org/10.2466/pms.101.2.409-412

Achenbach, T. M., & Rescorla, L. a. (2003). Manual for the ASEBA Adult Forms & Profiles. *English*. https://doi.org/10.1017/CBO9781107415324.004

Agargun, M. Y., Boysan, M., & Hanoglu, L. (2004). Sleeping position, dream emotions, and subjective sleep quality. *Sleep and Hypnosis*.

Akert, K., Koella, W. P., & Hess, R. (1952). Sleep produced by electrical stimulation of the thalamus. *The American Journal of Physiology*. https://doi.org/10.1152/ajplegacy.1951.168.1.260

Al-Backer, A., Al-Backer, N., Alzawad, M., Habibullah, H., & Bashir, S. (2018). The relationship between sleep and cognitive performance in Autism Spectrum Disorder (ASD): a pilot study. *Children*, *5*(11), 153.

Alati, R., Al Mamun, A., Williams, G. M., O'Callaghan, M., Najman, J. M., & Bor, W. (2006). In Utero Alcohol Exposure and Prediction of Alcohol Disorders in Early Adulthood. *Archives of General Psychiatry*, *63*(9), 1009. https://doi.org/10.1001/archpsyc.63.9.1009

Alberini, C. M., & Ledoux, J. E. (2013). Memory reconsolidation. *Current Biology*. https://doi.org/10.1016/j.cub.2013.06.046

Alberry, B. L., Castellani, C. A., & Singh, S. M. (2019). Hippocampal transcriptome analysis following maternal separation implicates altered RNA processing in a mouse model of fetal alcohol spectrum disorder. *BioRxiv*. https://doi.org/10.1101/685586

Alberry, B., & Singh, S. M. (2016). Developmental and behavioral consequences of early life maternal separation stress in a mouse model of fetal alcohol spectrum disorder. *Behavioural Brain Research*. https://doi.org/10.1016/j.bbr.2016.04.031

Alfano, C. A., Zakem, A. H., Costa, N. M., Taylor, L. K., & Weems, C. F. (2009). Sleep problems and their relation to cognitive factors, anxiety, and depressive symptoms in children and adolescents. *Depression and Anxiety*, *26*(6), 503–512. https://doi.org/10.1002/da.20443

Allely, C., & Gebbia, P. (2016). Studies Investigating Fetal Alcohol Spectrum Disorders in the Criminal Justice System: A Systematic PRISMA Review. *SOJ Psychology*, *2*(1), 1–11.

Allely, C. S., & Mukherjee, R. (2019). Suggestibility, false confessions and competency to stand trial in individuals with fetal alcohol spectrum disorders: current concerns and recommendations. *Journal of Criminal Psychology*. https://doi.org/10.1108/JCP-11-2019-050

Allison, C., Auyeung, B., & Baron-Cohen, S. (2012). Toward brief "red flags" for autism screening: The short Autism Spectrum Quotient and the short Quantitative Checklist in 1,000 cases and 3,000 controls. *Journal of the American Academy of Child and Adolescent Psychiatry*. https://doi.org/10.1016/j.jaac.2011.11.003

Alloway, T. P., & Gathercole, S. E. (2012). Working memory and neurodevelopmental disorders. In *Working Memory and Neurodevelopmental Disorders*. https://doi.org/10.4324/9780203013403

Alvaro, P. K., Roberts, R. M., & Harris, J. K. (2013). A Systematic Review Assessing Bidirectionality between Sleep Disturbances, Anxiety, and Depression. *Sleep*, *36*(7), 1059–1068. https://doi.org/10.5665/sleep.2810

Ameis, S. H., & Catani, M. (2015). Altered white matter connectivity as a neural substrate for social impairment in Autism Spectrum Disorder. *Cortex*. https://doi.org/10.1016/j.cortex.2014.10.014

American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (DSM). *CoDAS*.

American Psychological Association. (2020). Bias-Free Language. Retrieved April 8, 2020, from https://apastyle.apa.org/style-grammar-guidelines/bias-free-language/disability

Ames, C., & Fletcher-Watson, S. (2010). A review of methods in the study of attention in autism. *Developmental Review*. https://doi.org/10.1016/j.dr.2009.12.003

Anzulewicz, A., Sobota, K., & Delafield-Butt, J. T. (2016). Toward the Autism Motor Signature: Gesture patterns during smart tablet gameplay identify children with autism. *Scientific Reports*. https://doi.org/10.1038/srep31107

Armstrong, J. M., Ruttle, P. L., Klein, M. H., Essex, M. J., & Benca, R. M. (2014). Associations of Child Insomnia, Sleep Movement, and Their Persistence With Mental Health Symptoms in Childhood and Adolescence. *Sleep*. https://doi.org/10.5665/sleep.3656

Arora, T., Hussain, S., Hubert Lam, K. B., Lily Yao, G., Neil Thomas, G., & Taheri, S. (2013). Exploring the complex pathways among specific types of technology, self-reported sleep duration and body mass index in UK adolescents. *International Journal of Obesity*. https://doi.org/10.1038/ijo.2012.209

Aserinsky, E., & Kleitman, N. (1953). Regularly occurring periods of eye motility, and concomitant phenomena, during sleep. *Science*. https://doi.org/10.1126/science.118.3062.273

Ashworth, A., Hill, C. M., Karmiloff-Smith, A., & Dimitriou, D. (2014). Sleep enhances memory consolidation in children. *Journal of Sleep Research*, *23*(3), 302–308. https://doi.org/10.1111/jsr.12119

Ashworth, A., Hill, C. M., Karmiloff-Smith, A., & Dimitriou, D. (2017a). A cross-syndrome study of the differential effects of sleep on declarative memory consolidation in children with neurodevelopmental disorders. *Developmental Science*, *20*(2). https://doi.org/10.1111/desc.12383

Ashworth, A., Hill, C. M., Karmiloff-Smith, A., & Dimitriou, D. (2017b). A cross-syndrome study of the differential effects of

sleep on declarative memory consolidation in children with neurodevelopmental disorders. *Developmental Science*, *20*(2). https://doi.org/10.1111/desc.12383
Asperger, H. (1944). “Autistic psychopathy” in childhood. *In: Frith U, Ed. Autism and Asperger Syndrome. Cambridge: Cambridge University Press*.
Astill, R. G., Van der Heijden, K. B., Van Ijzendoorn, M. H., & Van Someren, E. J. W. (2012). Sleep, cognition, and behavioral problems in school-age children: A century of research meta-analyzed. *Psychological Bulletin*. https://doi.org/10.1037/a0028204
Astley, S. J. (2013). Validation of the fetal alcohol spectrum disorder (FASD) 4-Digit diagnostic code. *Journal of Population Therapeutics and Clinical Pharmacology*, *20*(3).
Astley, S. J., Aylward, E. H., Olson, H. C., Kerns, K., Brooks, A., Coggins, T. E., … Richards, T. (2009). Magnetic resonance imaging outcomes from a comprehensive magnetic resonance study of children with fetal alcohol spectrum disorders. *Alcoholism: Clinical and Experimental Research*. https://doi.org/10.1111/j.1530-0277.2009.01004.x
Attwood, A., Frith, U., & Hermelin, B. (1988). The understanding and use of interpersonal gestures by autistic and Down’s syndrome children. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/BF02211950
Baculis, B. C., Diaz, M. R., & Fernando Valenzuela, C. (2015). Third trimester-equivalent ethanol exposure increases anxiety-like behavior and glutamatergic transmission in the basolateral amygdala. *Pharmacology Biochemistry and Behavior*. https://doi.org/10.1016/j.pbb.2015.08.009
Baddeley, A. D., & Hitch, G. (1974). Working memory. *Psychology of Learning and Motivation - Advances in Research and Theory*. https://doi.org/10.1016/S0079-7421(08)60452-1
Baggio, S., Mussulini, B. H., de Oliveira, D. L., Gerlai, R., & Rico, E. P. (2018). Embryonic alcohol exposure leading to social avoidance and altered anxiety responses in adult zebrafish. *Behavioural Brain Research*. https://doi.org/10.1016/j.bbr.2017.08.039
Baglioni, C., Spiegelhalder, K., Lombardo, C., & Riemann, D. (2010). Sleep and emotions: A focus on insomnia. *Sleep Medicine Reviews*. https://doi.org/10.1016/j.smrv.2009.10.007
Ballesio, A., Aquino, M. R. J. V., Kyle, S. D., Ferlazzo, F., & Lombardo, C. (2019). Executive functions in insomnia disorder: A systematic review and exploratory meta-analysis. *Frontiers in Psychology*. https://doi.org/10.3389/fpsyg.2019.00101
Barakat, M., Doyon, J., Debas, K., Vandewalle, G., Morin, A., Poirier, G., … Carrier, J. (2011). Fast and slow spindle involvement in the consolidation of a new motor sequence. *Behavioural Brain Research*. https://doi.org/10.1016/j.bbr.2010.10.019
Barendse, E. M., Hendriks, M. P., Jansen, J. F., Backes, W. H., Hofman, P. A., Thoonen, G., … Aldenkamp, A. P. (2013). Working memory deficits in high-functioning adolescents with autism spectrum disorders: neuropsychological and neuroimaging correlates. *Journal of Neurodevelopmental Disorders*. https://doi.org/10.1186/1866-1955-5-14
Baron-Cohen, S., & Goodhart, F. (1994). The ‘seeing-leads-to-knowing’ deficit in autism: The Pratt and Bryant probe. *British Journal of Developmental Psychology*. https://doi.org/10.1111/j.2044-835x.1994.tb00642.x
Baron-Cohen, S., Leslie, A. M., & Frith, U. (1985). Does the autistic child have a “theory of mind” ? *Cognition*. https://doi.org/10.1016/0010-0277(85)90022-8
Baron-Cohen, S., Scott, F. J., Allison, C., Williams, J., Bolton, P., Matthews, F. E., & Brayne, C. (2009). Prevalence of autism-spectrum conditions: UK school-based population study. *The British Journal of Psychiatry : The Journal of Mental Science*, *194*(6), 500–509. https://doi.org/10.1192/bjp.bp.108.059345
Bean, T., Mooijart, A., Eurelings-Bontekoe, E., & Spinhoven, P. (2006). Validation of the child behavior checklist for guardians of unaccompanied refugee minors. *Children and Youth Services Review*, *28*(8), 867–887. https://doi.org/10.1016/j.childyouth.2005.09.002
Beebe, D. (2011). Cognitive, Behavioral, and Functional Consequences of Inadequate Sleep in Children and Adolescents. *Pediatric Clinics of North America*, *58*(3), 649–665. https://doi.org/10.1016/j.pcl.2011.03.002.Cognitive
Benington, J. H., & Craig Heller, H. (1995). Restoration of brain energy metabolism as the function of sleep. *Progress in Neurobiology*. https://doi.org/10.1016/0301-0082(94)00057-O
Berger, H. (1929). Das Elektrenkephalogramm des Menschen. *Archiv Für Psychiatrie Und Nervenkrankheiten*. https://doi.org/10.1007/BF01496966
Bhatara, V., Loudenberg, R., & Ellis, R. (2006). Association of attention deficit hyperactivity disorder and gestational alcohol exposure: an exploratory study. *Journal of Attention Disorders*, *9*(3), 515–522. https://doi.org/10.1177/1087054705283880
Bishop, S., Gahagan, S., & Lord, C. (2007). Re-examining the core features of autism: A comparison of autism spectrum disorder and fetal alcohol spectrum disorder. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. https://doi.org/10.1111/j.1469-7610.2007.01782.x
Blasi, A., Lloyd-Fox, S., Sethna, V., Brammer, M. J., Mercure, E., Murray, L., … Johnson, M. H. (2015). Atypical processing of voice sounds in infants at risk for autism spectrum disorder. *Cortex*. https://doi.org/10.1016/j.cortex.2015.06.015
Bleuler, E., & White, W. A. (1912). The theory of schizophrenic negativism. *Journal of Nervous and Mental Disease*. https://doi.org/10.1097/00005053-191203000-00011
Blumberg, M. S., Gall, A. J., & Todd, W. D. (2014). The development of sleep-wake rhythms and the search for elemental circuits in the infant brain. *Behavioral Neuroscience*. https://doi.org/10.1037/a0035891
BMJ Best Practice. (2017). British Medical Journal: FASD Best Practice. Retrieved September 9, 2017, from http://bestpractice.bmj.com/best-practice/monograph-pdf/1141.pdf
BMJ Best Practice. (2020a). Fetal alcohol spectrum disorders.

BMJ Best Practice. (2020b). Parasomnias in children. Retrieved January 8, 2020, from https://bestpractice.bmj.com/topics/en-gb/1177

Bodner, K. E., Williams, D. L., Engelhardt, C. R., & Minshew, N. J. (2014). A comparison of measures for assessing the level and nature of intelligence in verbal children and adults with autism spectrum disorder. *Research in Autism Spectrum Disorders*. https://doi.org/10.1016/j.rasd.2014.07.015

Boseck, J. J., Davis, A. S., Cassady, J. C., Finch, W. H., & Gelder, B. C. (2015). Cognitive and Adaptive Skill Profile Differences in Children With Attention-Deficit Hyperactivity Disorder With and Without Comorbid Fetal Alcohol Spectrum Disorder. *Applied Neuropsychology: Child*. https://doi.org/10.1080/21622965.2013.877392

Bower, C., Watkins, R. E., Mutch, R. C., Marriott, R., Freeman, J., Kippin, N. R., … Giglia, R. (2018). Fetal alcohol spectrum disorder and youth justice: A prevalence study among young people sentenced to detention in Western Australia. *BMJ Open*. https://doi.org/10.1136/bmjopen-2017-019605

Bowman, L. C. (2016). Developmental cognitive neuroscience. In *The Curated Reference Collection in Neuroscience and Biobehavioral Psychology*. https://doi.org/10.1016/B978-0-12-809324-5.23066-6

Boyce, R., Williams, S., & Adamantidis, A. (2017). REM sleep and memory. *Current Opinion in Neurobiology*. https://doi.org/10.1016/j.conb.2017.05.001

Brown, E. D., & Low, C. M. (2008). Chaotic living conditions and sleep problems associated with children's responses to academic challenge. *Journal of Family Psychology*, *22*(6), 920–923. https://doi.org/10.1037/a0013652

Brown, J. (2015). The challenges of caring for a child with FASD. *Adoption and Fostering*. https://doi.org/10.1177/0308575915599096

Brown, J., Freeman, N., Pickett, N., Watts, E., & Trnka, A. (2018). *FASD in Adult Populations: Clinical and Forensic Considerations*. https://doi.org/10.1007/978-3-319-71755-5_10

Brown, J., & Mather, M. (2016). *Foetal Alcohol Spectrum Disorder: Parenting a child with an invisible disability*. Oxford: FASD Trust.

Brown, J. P. (2013). *An Exploration of Social Communication in the Clinical and Educational Context* (Manchester Metropolitan University). Retrieved from https://e-space.mmu.ac.uk/326226/1/absolutely final thesis.pdf

Brown, W. J., Wilkerson, A. K., Boyd, S. J., Dewey, D., Mesa, F., & Bunnell, B. E. (2018). A review of sleep disturbance in children and adolescents with anxiety. *Journal of Sleep Research*. https://doi.org/10.1111/jsr.12635

Buckhalt, J. A., El-Sheikh, M., & Keller, P. (2007). Children's sleep and cognitive functioning: Race and socioeconomic status as moderators of effects. *Child Development*, *78*(1), 213–231. https://doi.org/10.1111/j.1467-8624.2007.00993.x

Burd, L. (2001). Children with Fetal Alcohol Syndrome: A Handbook for Parents and Teachers. *Grand Forks, ND: North Dakota Fetal Alcohol Syndrome Center.*

Burd, L. J. (2007). Interventions in FASD: We must do better. *Child: Care, Health and Development*, Vol. 33, pp. 398–400. https://doi.org/10.1111/j.1365-2214.2006.00696.x

Burd, L., Roberts, D., Olson, M., & Odendaal, H. (2007). Ethanol and the placenta: A review. *The Journal of Maternal-Fetal & Neonatal Medicine*, *20*(5), 361–375. https://doi.org/10.1080/14767050701298365

Burden, M. J., Jacobson, S. W., Sokol, R. J., & Jacobson, J. L. (2005). Effects of prenatal alcohol exposure on attention and working memory at 7.5 years of age. *Alcoholism: Clinical and Experimental Research*. https://doi.org/10.1097/01.ALC.0000156125.50577.EC

Calhoun, S. L., Pearl, A. M., Fernandez-Mendoza, J., Durica, K. C., Mayes, S. D., & Murray, M. J. (2019). Sleep Disturbances Increase the Impact of Working Memory Deficits on Learning Problems in Adolescents with High-Functioning Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-019-03928-y

Canivez, G. L., Watkins, M. W., & Dombrowski, S. C. (2017). Structural validity of the Wechsler Intelligence Scale for Children-Fifth Edition: Confirmatory factor analyses with the 16 primary and secondary subtests. *Psychological Assessment*. https://doi.org/10.1037/pas0000358

Cappuccio, F. P., Miller, M. A., Lockley, S. W., & Rajaratnam, S. M. W. (2018). Sleep, health, and society: From aetiology to public health. In *Sleep, Health, and Society: From Aetiology to Public Health*. https://doi.org/10.1093/oso/9780198778240.001.0001

Carskadon, M. A., & Dement, W. C. (2011). Normal Human Sleep : An Overview. *Principles and Practice of Sleep Medicine*, 16–26. https://doi.org/10.1016/B978-1-4160-6645-3.00141-9

Catterick, M., & Curran, L. (2014). *Understanding Fetal Alcohol Spectrum Disorder: A Guide to FASD for Parents, Carers and Professionals*. JKP Essentials Series.

CDC Centers for Disease Control. (2005). FASD: Guidelines for referral and diagnosis.

Charman, T., Jones, C. R. G., Pickles, A., Simonoff, E., Baird, G., & Happé, F. (2011). Defining the cognitive phenotype of autism. *Brain Research*. https://doi.org/10.1016/j.brainres.2010.10.075

Chase, R. M., & Pincus, D. B. (2011). Sleep-Related Problems in Children and Adolescents With Anxiety Disorders. *Behavioral Sleep Medicine*. https://doi.org/10.1080/15402002.2011.606768

Chasnoff, I. J., Wells, A. M., & King, L. (2015). Misdiagnosis and Missed Diagnoses in Foster and Adopted Children With Prenatal Alcohol Exposure. *PEDIATRICS*, *135*(2), 264–270. https://doi.org/10.1542/peds.2014-2171

Chatburn, A., Coussens, S., Lushington, K., Kennedy, D., Baumert, M., & Kohler, M. (2013). Sleep Spindle Activity and Cognitive Performance in Healthy Children. *Sleep*. https://doi.org/10.5665/sleep.2380

Chaudhuri, K. R., Pal, S., DiMarco, A., Whately-Smith, C., Bridgman, K., Mathew, R., … Trenkwalder, C. (2002). The Parkinson's disease sleep scale: A new instrument for assessing sleep and nocturnal disability in Parkinson's disease. *Journal of Neurology Neurosurgery and Psychiatry*. https://doi.org/10.1136/jnnp.73.6.629

Chee, M. W. L., & Choo, W. C. (2004). Functional imaging of working memory after 24 hr of total sleep deprivation. *Journal of Neuroscience*. https://doi.org/10.1523/JNEUROSCI.0007-04.2004
Chen, M., & Olson, H. (2006). Sleepless in Seattle: Preliminary data suggesting sleep disorders in those with FASD. *Research Society for Alcoholism, Fetal Alcohol Spectrum Disorders Study Group. Conference Paper.*
Chen, M L, Olson, H. C., Picciano, J. F., Starr, J. R., & Owens, J. (2012). Sleep problems in children with fetal alcohol spectrum disorders. *Journal of Clinical Sleep Medicine*, *8*(4), 421–429. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed10&AN=2012572194%5Cnhttp://lib.exeter.ac.uk:4556/resserv?sid=OVID:embase&id=pmid:&id=doi:10.5664/jcsm.2038&issn=1550-9389&isbn=&volume=8&issue=4&spage=421&pages=421-429&date=2012&tit
Chen, Maida Lynn, & Olson, H. C. (2015). Sleep in Fetal Alcohol Spectrum Disorders. In *Modulation of Sleep by Obesity, Diabetes, Age, and Diet* (pp. 313–317). Elsevier Ltd.
Chen, Olson, Picciano, Starr, & Owens. (2012). Sleep problems in children with fetal alcohol spectrum disorders. *Journal of Clinical Sleep Medicine*, *8*(4), 421–429. https://doi.org/10.5664/jcsm.2038
Chevallier, C., Kohls, G., Troiani, V., Brodkin, E. S., & Schultz, R. T. (2012). The social motivation theory of autism. *Trends in Cognitive Sciences*. https://doi.org/10.1016/j.tics.2012.02.007
Christiansen, D. M. (2015). Examining Sex and Gender Differences in Anxiety Disorders. In *A Fresh Look at Anxiety Disorders*. https://doi.org/10.5772/60662
Cohen, J. (2013). Statistical Power Analysis for the Behavioral Sciences. In *Statistical Power Analysis for the Behavioral Sciences*. https://doi.org/10.4324/9780203771587
Cohen, S., Conduit, R., Lockley, S. W., Rajaratnam, S. M., & Cornish, K. M. (2014). The relationship between sleep and behavior in autism spectrum disorder (ASD): A review. *Journal of Neurodevelopmental Disorders*. https://doi.org/10.1186/1866-1955-6-44
Cook, J. L., Green, C. R., Lilley, C. M., Anderson, S. M., Baldwin, M. E., Chudley, A. E., … Rosales, T. (2016). Fetal alcohol spectrum disorder: A guideline for diagnosis across the lifespan. *CMAJ*. https://doi.org/10.1503/cmaj.141593
Corcoran, K., Crusius, J., & Mussweiler, T. (2011). Social Comparison : Motives , Standards , and Mechanisms. *Theories in Social Psychology*, (5), 119–139. Retrieved from http://books.google.com/books?id=DnVBDPEFFCQC&printsec=frontcover&dq=Theories+in+Social+psychology&hl=&cd=1&source=gbs_api%5Cnhttp://social-cognition.uni-koeln.de/scc4/documents/Social_comparison.pdf
Coriale, G., Fiorentino, D., DiLauro, F., Marchitelli, R., Scalese, B., Fiore, M., … Ceccanti, M. (2013). Fetal Alcohol Spectrum Disorder (FASD): neurobehavioral profile, indications for diagnosis and treatment. *La Rivista Psichiatria*, *48*(5), 359–369.
Cortesi, F., Giannotti, F., Ivanenko, A., & Johnson, K. (2010). Sleep in children with autistic spectrum disorder. *Sleep Medicine*. https://doi.org/10.1016/j.sleep.2010.01.010
Cotton, S., & Richdale, A. (2006). Brief report: Parental descriptions of sleep problems in children with autism, Down syndrome, and Prader-Willi syndrome. *Research in Developmental Disabilities*. https://doi.org/10.1016/j.ridd.2004.12.003
Courchesne, E., Mouton, P. R., Calhoun, M. E., Semendeferi, K., Ahrens-Barbeau, C., Hallet, M. J., … Pierce, K. (2011). Neuron number and size in prefrontal cortex of children with autism. *JAMA - Journal of the American Medical Association*. https://doi.org/10.1001/jama.2011.1638
Courchesne, V., Meilleur, A. A. S., Poulin-Lord, M. P., Dawson, M., & Soulières, I. (2015). Autistic children at risk of being underestimated: School-based pilot study of a strength-informed assessment. *Molecular Autism*. https://doi.org/10.1186/s13229-015-0006-3
Cox, R. C., & Olatunji, B. O. (2020). Sleep in the anxiety-related disorders: A meta-analysis of subjective and objective research. *Sleep Medicine Reviews*. https://doi.org/10.1016/j.smrv.2020.101282
Craig, J. (2001). Drawing ability in autism: A window into the imagination. *Israel Journal of Psychiatry and Related Sciences*.
Crespi, B., Leach, E., Dinsdale, N., Mokkonen, M., & Hurd, P. (2016). Imagination in human social cognition, autism, and psychotic-affective conditions. *Cognition*. https://doi.org/10.1016/j.cognition.2016.02.001
Crocker, N., Riley, E. P., & Mattson, S. N. (2015). Visual-spatial abilities relate to mathematics achievement in children with heavy prenatal alcohol exposure. *Neuropsychology*. https://doi.org/10.1037/neu0000094
Dahl RE. (1999). The consequences of insufficient sleep for adolescents - Links between sleep and emotional regulation. *Phi Delta Kappan*, *80*(5), 179–189. https://doi.org/10.2307/20439447
Davidovitch, M., Glick, L., Holtzman, G., Tirosh, E., & Safir, M. P. (2000). Developmental regression in autism: Maternal perception. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1023/A:1005403421141
Davidson, C., O'Hare, A., Mactaggart, F., Green, J., Young, D., Gillberg, C., & Minnis, H. (2015). Social relationship difficulties in autism and reactive attachment disorder: Improving diagnostic validity through structured assessment. *Research in Developmental Disabilities*, *40*, 63–72. https://doi.org/10.1016/j.ridd.2015.01.007
Davis, K. F., Parker, K. P., & Montgomery, G. L. (2004). Sleep in infants and young children. *Journal of Pediatric Health Care*. https://doi.org/10.1016/s0891-5245(03)00150-0
Davis, P. E., Simon, H., Meins, E., & Robins, D. L. (2018). Imaginary Companions in Children with Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-018-3540-y
Davis, T., White, S., & Ollendick, T. (2014). Handbook of autism and anxiety. In *Autism and child psychopathology series.* https://doi.org/http://dx.doi.org/10.1007/978-3-319-06796-4
Dawson, G., Meltzoff, A. N., Osterling, J., Rinaldi, J., & Brown, E. (1998). Children with autism fail to orient to naturally

occurring social stimuli. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1023/A:1026043926488
de Andrés, I., Garzón, M., & Reinoso-Suárez, F. (2011). Functional anatomy of non-REM sleep. *Frontiers in Neurology*. https://doi.org/10.3389/fneur.2011.00070
DeGangi, G. A. (2017). Problems of Self-Regulation in Children: A Longitudinal Case Study of a Child from Infancy to Adulthood. *Journal of Psychology & Clinical Psychiatry*. https://doi.org/10.15406/jpcpy.2017.07.00428
Dehlink, E. (2016). Update on paediatric obstructive sleep apnoea. *J Thorac Dis*.
DeQuinzio, J. A., Poulson, C. L., Townsend, D. B., & Taylor, B. A. (2016). Social Referencing and Children with Autism. *Behavior Analyst*. https://doi.org/10.1007/s40614-015-0046-1
Devnani, P., & Hegde, A. (2015). Autism and sleep disorders. *Journal of Pediatric Neurosciences*. https://doi.org/10.4103/1817-1745.174438
Diamond, A. (2013). Executive Functions. *Annual Review of Psychology*. https://doi.org/10.1146/annurev-psych-113011-143750
Díaz-Román, A., Zhang, J., Delorme, R., Beggiato, A., & Cortese, S. (2018). Sleep in youth with autism spectrum disorders: Systematic review and meta-analysis of subjective and objective studies. *Evidence-Based Mental Health*, *21*(4), 146. https://doi.org/10.1136/ebmental-2018-300037
Diekelmann, S., Wilhelm, I., & Born, J. (2009). The whats and whens of sleep-dependent memory consolidation. *Sleep Medicine Reviews*. https://doi.org/10.1016/j.smrv.2008.08.002
Diener, M. L., Wright, C. A., Smith, K. N., & Wright, S. D. (2014). Assessing Visual-Spatial Creativity in Youth on the Autism Spectrum. *Creativity Research Journal*. https://doi.org/10.1080/10400419.2014.929421
DiPietro, J. A. (2016). Prenatal development. In *The Curated Reference Collection in Neuroscience and Biobehavioral Psychology*. https://doi.org/10.1016/B978-0-12-809324-5.21831-2
Doran, S. M., Van Dongen, H. P. A., & Dinges, D. F. (2001). Sustained attention performance during sleep deprivation: Evidence of state instability. *Archives Italiennes de Biologie*. https://doi.org/10.4449/aib.v139i3.503
Dunn, Dunn, Styles, & Sewell. (2009). *British Picture Vocabulary Scale: 3rd Edition.* GL Assessment.
Dunn, W. (1997). The impact of sensory processing abilities on the daily lives of young children and their families: A conceptual model. *Infants and Young Children*. https://doi.org/10.1097/00001163-199704000-00005
Duvekot, J., van der Ende, J., Verhulst, F. C., Slappendel, G., van Daalen, E., Maras, A., & Greaves-Lord, K. (2017). Factors influencing the probability of a diagnosis of autism spectrum disorder in girls versus boys. *Autism*. https://doi.org/10.1177/1362361316672178
Earnest, D. J., Chen, W. J., & West, J. R. (2001). Developmental alcohol and circadian clock function. *Alcohol Res Health*, *25*(2), 136–140.
Elrod, M. G., & Hood, B. S. (2015). Sleep differences among children with autism spectrum disorders and typically developing peers: A Meta-analysis. *Journal of Developmental and Behavioral Pediatrics*. https://doi.org/10.1097/DBP.0000000000000140
Elsabbagh, M., Divan, G., Koh, Y. J., Kim, Y. S., Kauchali, S., Marcín, C., … Fombonne, E. (2012). Global Prevalence of Autism and Other Pervasive Developmental Disorders. *Autism Research*. https://doi.org/10.1002/aur.239
Elsabbagh, M., Volein, A., Csibra, G., Holmboe, K., Garwood, H., Tucker, L., … Johnson, M. H. (2009). Neural Correlates of Eye Gaze Processing in the Infant Broader Autism Phenotype. *Biological Psychiatry*. https://doi.org/10.1016/j.biopsych.2008.09.034
Elwood, P. C., Bayer, A. J., Fish, M., Pickering, J., Mitchell, C., & Gallacher, J. E. J. (2011). Sleep disturbance and daytime sleepiness predict vascular dementia. *Journal of Epidemiology and Community Health*. https://doi.org/10.1136/jech.2009.100503
Enns, L. N., & Taylor, N. M. (2018). Factors predictive of a fetal alcohol spectrum disorder: Neuropsychological assessment. *Child Neuropsychology*, 1–23. https://doi.org/10.1080/09297049.2016.1251894
Esbensen, A. J., & Schwichtenberg, A. J. (2016). Sleep in Neurodevelopmental Disorders. *International Review of Research in Developmental Disabilities*. https://doi.org/10.1016/bs.irrdd.2016.07.005
Espie, C. A., & Morin, C. M. (2012). The Oxford Handbook of Sleep and Sleep Disorders. In *Oxford University Press*. https://doi.org/10.1093/oxfordhb/9780195376203.001.0001
Essau, C. A., Muris, P., & Ederer, E. M. (2002). Reliability and validity of the Spence Children's Anxiety Scale and the Screen for Child Anxiety Related Emotional Disorders in German children. *Journal of Behavior Therapy and Experimental Psychiatry*, *33*(1), 1–18. https://doi.org/10.1016/S0005-7916(02)00005-8
Factor, R. S., Condy, E. E., Farley, J. P., & Scarpa, A. (2016). Brief Report: Insistence on Sameness, Anxiety, and Social Motivation in Children with Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-016-2781-x
Fadini, C. C., Lamônica, D. A., Fett-Conte, A. C., Osório, E., Zuculo, G. M., Giacheti, C. M., & Pinato, L. (2015). Influence of sleep disorders on the behavior of individuals with autism spectrum disorder. *Frontiers in Human Neuroscience*. https://doi.org/10.3389/fnhum.2015.00347
Fallone, G., Acebo, C., Arnedt, J. T., Seifer, R., & Carskadon, M. A. (2001). Effects of acute sleep restriction on behavior, sustained attention, and response inhibition in children. *Perceptual and Motor Skills*. https://doi.org/10.2466/pms.2001.93.1.213
Farnsworth, B. (2018). Eye Tracking and Autism. Current and Future Research.
Farrell, L. J. [Ed], Ollendick, T. H. [Ed], & Muris, P. [Ed]. (2019). Innovations in CBT for childhood anxiety, OCD, and PTSD: Improving access and outcomes. *Cambridge University Press*.

https://doi.org/http://dx.doi.org/10.1017/9781108235655
Fast, D. K., & Conry, J. (2009). Fetal alcohol spectrum disorders and the criminal justice system. *Developmental Disabilities Research Reviews*, Vol. 15, pp. 250–257. https://doi.org/10.1002/ddrr.66
Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*. https://doi.org/10.3758/BF03193146
Fernandez, F., Lu, D., Ha, P., Costacurta, P., Chavez, R., Heller, H. C., & Ruby, N. F. (2014). Dysrhythmia in the suprachiasmatic nucleus inhibits memory processing. *Science*. https://doi.org/10.1126/science.1259652
Ferraro, F. R. (2016). No evidence of reaction time slowing in autism spectrum disorder. *Autism*. https://doi.org/10.1177/1362361314559986
Fidan, T., & Fidan, V. (2008). The impact of adenotonsillectomy on attention-deficit hyperactivity and disruptive behavioral symptoms. *The Eurasian Journal of Medicine*, *40*(1), 14–17. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/25610016%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4261322
Field, A. (2018). Discovering statistics using IBM SPSS statistics. In *Statistics*.
Fletcher-Watson, S., & Happé, F. (2019a). Autism at the cognitive level. In *Routledge* (p. 194). https://doi.org/10.4324/9781315101699-8
Fletcher-Watson, S., & Happé, F. (2019b). Autism at the cognitive level. In *Autism*. https://doi.org/10.4324/9781315101699-8
Fletcher, F. E., Conduit, R., Foster-Owens, M. D., Rinehart, N. J., Rajaratnam, S. M. W., & Cornish, K. M. (2018). The Association Between Anxiety Symptoms and Sleep in School-Aged Children: A Combined Insight From the Children's Sleep Habits Questionnaire and Actigraphy. *Behavioral Sleep Medicine*. https://doi.org/10.1080/15402002.2016.1180522
Fletcher, F. E., Knowland, V., Walker, S., Gaskell, M. G., Norbury, C., & Henderson, L. M. (2019). Atypicalities in sleep and semantic consolidation in autism. *Developmental Science*. https://doi.org/10.1111/desc.12906
Fraley, R. C., & Vazire, S. (2014). The N-pact factor: Evaluating the quality of empirical journals with respect to sample size and statistical power. *PLoS ONE*. https://doi.org/10.1371/journal.pone.0109019
Frank, M. G. (2018). *The Role of Glia in Sleep Regulation and Function*. https://doi.org/10.1007/164_2017_87
Frank, M. G., & Heller, H. C. (2003). The ontogeny of mammalian sleep: A reappraisal of alternative hypotheses. *Journal of Sleep Research*. https://doi.org/10.1046/j.1365-2869.2003.00339.x
Frye, S., Fernandez-Mendoza, J., Calhoun, S., Vgontzas, A., Liao, D., & Bixler, E. (2017). Role of periodic limb movemements during sleep in adolecents with Attention Deficit Hyperactivity Disorder: Differential association with internalising vs externalising behaviors. *Sleep*. https://doi.org/10.1093/sleepj/zsx050.932
Gabriels, R. L., Cuccaro, M. L., Hill, D. E., Ivers, B. J., & Goldson, E. (2005). Repetitive behaviors in autism: Relationships with associated clinical features. *Research in Developmental Disabilities*. https://doi.org/10.1016/j.ridd.2004.05.003
Gagnier, K. R., Moore, T. E., & Green, J. M. (2011). A need for closer examination of fasd by the criminal justice system: Has the call been answered? *Journal of Population Therapeutics and Clinical Pharmacology*, Vol. 18.
Gais, S., & Born, J. (2004). Declarative memory consolidation: Mechanisms acting during human sleep. *Learning and Memory*. https://doi.org/10.1101/lm.80504
Gareri, J., Lynn, H., Handley, M., Rao, C., & Koren, G. (2008). Prevalence of fetal ethanol exposure in a regional population-based sample by meconium analysis of fatty acid ethyl esters. *Therapeutic Drug Monitoring*, *30*(2), 239–245. https://doi.org/10.1097/FTD.0b013e318167cfe5
Garfin, D. G., & McCallon, D. (1988). Validity and reliability of the Childhood Autism Rating Scale with autistic adolescents. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/BF02212193
Gautam, P., Nuñez, S. C., Narr, K. L., Mattson, S. N., May, P. A., Adnams, C. M., … Sowell, E. R. (2015). Developmental trajectories for visuo-spatial attention are altered by prenatal alcohol exposure: A longitudinal FMRI study. *Cerebral Cortex*. https://doi.org/10.1093/cercor/bhu162
Gauthier, T. W., Mohan, S. S., Gross, T. S., Harris, F. L., Guidot, D. M., & Brown, L. A. S. (2015). Placental fatty acid ethyl esters are elevated with maternal alcohol use in pregnancies complicated by prematurity. *PLoS ONE*, *10*(5). https://doi.org/10.1371/journal.pone.0126552
Giannotti, F., Cortesi, F., Cerquiglini, A., Vagnoni, C., & Valente, D. (2011). Sleep in children with autism with and without autistic regression. *Journal of Sleep Research*. https://doi.org/10.1111/j.1365-2869.2010.00882.x
Giannotti, F., Cortesi, F., Sebastiani, T., & Ottaviano, S. (2002). Circadian preference, sleep and daytime behaviour in adolescence. *Journal of Sleep Research*, *11*(3), 191–199. https://doi.org/10.1046/j.1365-2869.2002.00302.x
Glaser, N., & Styne, D. (2017). Weighing the Causal Evidence That Associates Short Sleep Duration With Obesity. *Pediatrics*. https://doi.org/10.1542/peds.2017-2015
Glass, L., & Mattson, S. N. (2017). Fetal Alcohol Spectrum Disorders: a Case Study. *Journal of Pediatric Neuropsychology*. https://doi.org/10.1007/s40817-016-0027-7
Glass, L., Ware, A. L., & Mattson, S. N. (2014). Neurobehavioral, neurologic, and neuroimaging characteristics of fetal alcohol spectrum disorders. In *Handbook of Clinical Neurology*. https://doi.org/10.1016/B978-0-444-62619-6.00025-2
Gliga, T., Bedford, R., Charman, T., Johnson, M. H., Baron-Cohen, S., Bolton, P., … Tucker, L. (2015). Enhanced Visual Search in Infancy Predicts Emerging Autism Symptoms. *Current Biology*. https://doi.org/10.1016/j.cub.2015.05.011
Goel, N., Basner, M., Rao, H., & Dinges, D. F. (2013). Circadian rhythms, sleep deprivation, and human performance.

Progress in Molecular Biology and Translational Science. https://doi.org/10.1016/B978-0-12-396971-2.00007-5
Goel, N., Rao, H., Durmer, J. S., & Dinges, D. F. (2009). Neurocognitive consequences of sleep deprivation. *Seminars in Neurology*, Vol. 29, pp. 320–339. https://doi.org/10.1055/s-0029-1237117
Gokdemir, Y., & Ersu, R. (2016). Sleep disordered breathing in childhood. *European Respiratory Review : An Official Journal of the European Respiratory Society*. https://doi.org/10.1183/16000617.0081-2015
Gold, A. K., & Sylvia, L. G. (2016). The role of sleep in bipolar disorder. *Nature and Science of Sleep*. https://doi.org/10.2147/NSS.S85754
Goldschmied, J. R. (2018). The effects of sleep manipulation on emotional processing and mood. *Dissertation Abstracts International: Section B: The Sciences and Engineering*.
Goldstein, S., Naglieri, J. A., Princiotta, D., & Otero, T. M. (2014). Introduction: A history of executive functioning as a theoretical and clinical construct. In *Handbook of Executive Functioning*. https://doi.org/10.1007/978-1-4614-8106-5_1
Gomot, M., Belmonte, M. K., Bullmore, E. T., Bernard, F. A., & Baron-Cohen, S. (2008). Brain hyper-reactivity to auditory novel targets in children with high-functioning autism. *Brain*. https://doi.org/10.1093/brain/awn172
Goril, S., Zalai, D., Scott, L., & Shapiro, C. M. (2016). Sleep and melatonin secretion abnormalities in children and adolescents with fetal alcohol spectrum disorders. *Sleep Medicine*, *23*, 59–64. https://doi.org/10.1016/j.sleep.2016.06.002
Goril, Scott, & Shapiro. (2012). The patterns of sleep disorders and circadian rhythm disruptions in children and adolescents with fetal alcohol spectrum disorders. *Sleep*, *35*(SUPPL. 1), A378. Retrieved from http://www.journalsleep.org/Resources/Documents/2012abstractsupplement.pdf%5Cnhttp://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed12&NEWS=N&AN=71515232
Górriz, J. M., Ramírez, J., Segovia, F., Martínez, F. J., Lai, M. C., Lombardo, M. V., … Suckling, J. (2019). A Machine Learning Approach to Reveal the NeuroPhenotypes of Autisms. *International Journal of Neural Systems*. https://doi.org/10.1142/S0129065718500582
Green, C. R., Mihic, A. M., Nikkel, S. M., Stade, B. C., Rasmussen, C., Munoz, D. P., & Reynolds, J. N. (2009). Executive function deficits in children with fetal alcohol spectrum disorders (FASD) measured using the Cambridge Neuropsychological Tests Automated Battery (CANTAB). *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *50*(6), 688–697. https://doi.org/10.1111/j.1469-7610.2008.01990.x
Green, D. G., & Swets, J. A. (1966). Signal detection theory and psychophysics. In *New York, NY: John Wiley and Sons Inc.* https://doi.org/10.1901/jeab.1969.12-475
Greenbaum, R. L., Stevens, S. A., Nash, K., Koren, G., & Rovet, J. (2009). Social cognitive and emotion processing abilities of children with fetal alcohol spectrum disorders: A comparison with attention deficit hyperactivity disorder. *Alcoholism: Clinical and Experimental Research*, *33*(10), 1656–1670. https://doi.org/10.1111/j.1530-0277.2009.01003.x
Gregory, A. M., Caspi, A., Eley, T. C., Moffitt, T. E., O'Connor, T. G., & Poulton, R. (2005). Prospective longitudinal associations between persistent sleep problems in childhood and anxiety and depression disorders in adulthood. *Journal of Abnormal Child Psychology*. https://doi.org/10.1007/s10802-005-1824-0
Gregory, A. M., & Eley, T. C. (2005). Sleep problems, anxiety and cognitive style in school-aged children. *Infant and Child Development*. https://doi.org/10.1002/icd.409
Gregory, A. M., & Sadeh, A. (2012). Sleep, emotional and behavioral difficulties in children and adolescents. *Sleep Medicine Reviews*, Vol. 16, pp. 129–136. https://doi.org/10.1016/j.smrv.2011.03.007
Gregory, G., Reddy, V., & Young, C. (2015). Identifying children who are at risk of FASD in Peterborough: working in a community clinic without access to gold standard diagnosis. *Adoption & Fostering*, *39*(3), 225–234. https://doi.org/10.1177/0308575915594985
Grelotti, D. J., Klin, A. J., Gauthier, I., Skudlarski, P., Cohen, D. J., Gore, J. C., … Schultz, R. T. (2005). fMRI activation of the fusiform gyrus and amygdala to cartoon characters but not to faces in a boy with autism. *Neuropsychologia*. https://doi.org/10.1016/j.neuropsychologia.2004.06.015
Greydanus, D. E. (2018). Sleep disorders in children and adolescents. In *Chronic Disease and Disability: The Pediatric Lung*. https://doi.org/10.1192/apt.bp.114.014050
Gunes, S., Ekinci, O., Feyzioglu, A., Ekinci, N., & Kalinli, M. (2019). Sleep problems in children with autism spectrum disorder: Clinical correlates and the impact of attention deficit hyperactivity disorder. *Neuropsychiatric Disease and Treatment*. https://doi.org/10.2147/NDT.S195738
Ha, S., Sohn, I.-J., Kim, N., Sim, H. J., & Cheon, K.-A. (2015). Characteristics of Brains in Autism Spectrum Disorder: Structure, Function and Connectivity across the Lifespan. *Experimental Neurobiology*. https://doi.org/10.5607/en.2015.24.4.273
Habeck, C., Rakitin, B. C., Moeller, J., Scarmeas, N., Zarahn, E., Brown, T., & Stern, Y. (2004). An event-related fMRI study of the neurobehavioral impact of sleep deprivation on performance of a delayed-match-to-sample task. *Cognitive Brain Research*. https://doi.org/10.1016/j.cogbrainres.2003.10.019
Habib, A., Harris, L., Pollick, F., & Melville, C. (2019). A meta-analysis of working memory in individuals with autism spectrum disorders. *PLoS ONE*. https://doi.org/10.1371/journal.pone.0216198
Hale, L., & Guan, S. (2015). Screen time and sleep among school-aged children and adolescents: A systematic literature review. *Sleep Medicine Reviews*. https://doi.org/10.1016/j.smrv.2014.07.007
Hanifin, J. P., Lockley, S. W., Cecil, K., West, K., Jablonski, M., Warfield, B., … Brainard, G. C. (2019). Randomized trial of

polychromatic blue-enriched light for circadian phase shifting, melatonin suppression, and alerting responses. *Physiology and Behavior*. https://doi.org/10.1016/j.physbeh.2018.10.004

Hannant, P. (2018). Receptive language is associated with visual perception in typically developing children and sensorimotor skills in autism spectrum conditions. *Human Movement Science*. https://doi.org/10.1016/j.humov.2018.03.005

Hanratty, J., Livingstone, N., Robalino, S., Terwee, C. B., Glod, M., Oono, I. P., … McConachie, H. (2015). Systematic review of the measurement properties of tools used to measure behaviour problems in young children with autism. *PLoS ONE*. https://doi.org/10.1371/journal.pone.0144649

Happe, F., & Fletcher Watson, S. (2019). *Autism: a new introduction to psychological theory and current debate* (2nd ed.). Routledge.

Havdahl, K. A., von Tetzchner, S., Huerta, M., Lord, C., & Bishop, S. L. (2016). Utility of the Child Behavior Checklist as a Screener for Autism Spectrum Disorder. *Autism Research*. https://doi.org/10.1002/aur.1515

Hellemans, K. G. C., Sliwowska, J. H., Verma, P., & Weinberg, J. (2010). Prenatal alcohol exposure: Fetal programming and later life vulnerability to stress, depression and anxiety disorders. *Neuroscience and Biobehavioral Reviews*. https://doi.org/10.1016/j.neubiorev.2009.06.004

Hellemans, K. G. C., Verma, P., Yoon, E., Yu, W. K., Young, A. H., & Weinberg, J. (2010). Prenatal alcohol exposure and chronic mild stress differentially alter depressive- and anxiety-like behaviors in male and female offspring. *Alcoholism: Clinical and Experimental Research*. https://doi.org/10.1111/j.1530-0277.2009.01132.x

Hill, C. M., Hogan, A. M., & Karmiloff-Smith, A. (2007). To sleep, perchance to enrich learning? *Archives of Disease in Childhood*, *92*(7), 637–643. https://doi.org/10.1136/adc.2006.096156

Hill, E. L. (2004). Executive dysfunction in autism. *Trends in Cognitive Sciences*. https://doi.org/10.1016/j.tics.2003.11.003

Himes, S. K., Dukes, K. A., Tripp, T., Petersen, J. M., Raffo, C., Burd, L., … Huestis, M. A. (2015). Clinical sensitivity and specificity of meconium fatty acid ethyl ester, ethyl glucuronide, and ethyl sulfate for detecting maternal drinking during pregnancy. *Clinical Chemistry*, *61*(3), 523–532. https://doi.org/10.1373/clinchem.2014.233718

Hirata, I., Mohri, I., Kato-Nishimura, K., Tachibana, M., Kuwada, A., Kagitani-Shimono, K., … Taniike, M. (2016). Sleep problems are more frequent and associated with problematic behaviors in preschoolers with autism spectrum disorder. *Research in Developmental Disabilities*. https://doi.org/10.1016/j.ridd.2015.11.002

Hirvikoski, T., Mittendorfer-Rutz, E., Boman, M., Larsson, H., Lichtenstein, P., & Bölte, S. (2016). Premature mortality in autism spectrum disorder. *British Journal of Psychiatry*. https://doi.org/10.1192/bjp.bp.114.160192

Hiscock, H., Sciberras, E., Mensah, F., Gerner, B., Efron, D., Khano, S., & Oberklaid, F. (2015). Impact of a behavioural sleep intervention on symptoms and sleep in children with attention deficit hyperactivity disorder, and parental mental health: Randomised controlled trial. *British Medical Journal*. https://doi.org/10.1136/bmj.h68

Hjorth, M. F., Sørensen, L. B., Andersen, R., Dyssegaard, C. B., Ritz, C., Tetens, I., … Sjödin, A. (2016). Normal weight children have higher cognitive performance – Independent of physical activity, sleep, and diet. *Physiology and Behavior*. https://doi.org/10.1016/j.physbeh.2016.08.021

Hodge, D., Carollo, T. M., Lewin, M., Hoffman, C. D., & Sweeney, D. P. (2014). Sleep patterns in children with and without autism spectrum disorders: Developmental comparisons. *Research in Developmental Disabilities*. https://doi.org/10.1016/j.ridd.2014.03.037

Hoedlmoser, K., Heib, D. P. J., Roell, J., Peigneux, P., Sadeh, A., Gruber, G., & Schabus, M. (2014). Slow Sleep Spindle Activity, Declarative Memory, and General Cognitive Abilities in Children. *Sleep*. https://doi.org/10.5665/sleep.4000

Holdnack, J. A. (2019). The development, expansion, and future of the WAIS-IV as a cornerstone in comprehensive cognitive assessments. In *Handbook of Psychological Assessment*. https://doi.org/10.1016/b978-0-12-802203-0.00004-3

Holley, S., Hill, C. M., & Stevenson, J. (2010). A comparison of actigraphy and parental report of sleep habits in typically developing children aged 6 to 11 years. *Behavioral Sleep Medicine*. https://doi.org/10.1080/15402000903425462

Hoppenbrouwers, T., & Sterman, M. B. (1975). Development of sleep state patterns in the kitten. *Experimental Neurology*. https://doi.org/10.1016/0014-4886(75)90062-X

Hoppenbrouwers, T., Ugartechea, J. C., Combs, D., Hodgman, J. E., Harper, R. M., & Sterman, M. B. (1978). Studies of maternal-fetal interaction during the last trimester of pregnancy: Ontogenesis of the basic rest-activity cycle. *Experimental Neurology*. https://doi.org/10.1016/0014-4886(78)90186-3

Horder, J., Andersson, M., Mendez, M. A., Singh, N., Tangen, Ä., Lundberg, J., … Borg, J. (2018). GABAA receptor availability is not altered in adults with autism spectrum disorder or in mouse models. *Science Translational Medicine*. https://doi.org/10.1126/scitranslmed.aam8434

Horne, R. S., Wijayaratne, P., Nixon, G. M., & Walter, L. M. (2019). Sleep and sleep disordered breathing in children with down syndrome: Effects on behaviour, neurocognition and the cardiovascular system. *Sleep Medicine Reviews*. https://doi.org/10.1016/j.smrv.2018.11.002

Howe, D. (2006). Disabled children, parent-child interaction and attachment. *Child and Family Social Work*, *11*(2), 95–106. https://doi.org/10.1111/j.1365-2206.2006.00397.x

Hoyme, H. E., Kalberg, W. O., Elliott, A. J., Blankenship, J., Buckley, D., Marais, A. S., … May, P. A. (2016). Updated clinical guidelines for diagnosing fetal alcohol spectrum disorders. *Pediatrics*. https://doi.org/10.1542/peds.2015-4256

Huber, R., & Born, J. (2014). Sleep, synaptic connectivity, and hippocampal memory during early development. *Trends in Cognitive Sciences*. https://doi.org/10.1016/j.tics.2013.12.005

Huber, R., Ghilardi, M. F., Massimini, M., & Tononi, G. (2004). Local sleep and learning. *Nature*.

https://doi.org/10.1038/nature02663
Hudson, A. N., Van Dongen, H. P. A., & Honn, K. A. (2020). Sleep deprivation, vigilant attention, and brain function: a review. *Neuropsychopharmacology*. https://doi.org/10.1038/s41386-019-0432-6
Hughes, C., Russell, J., & Robbins, T. W. (1994). Evidence for executive dysfunction in autism. *Neuropsychologia*. https://doi.org/10.1016/0028-3932(94)90092-2
Hull, L., Petrides, K. V., & Mandy, W. (2020). The Female Autism Phenotype and Camouflaging: a Narrative Review. *Review Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s40489-020-00197-9
Humphreys, J. S., Gringras, P., Blair, P. S., Scott, N., Henderson, J., Fleming, P. J., & Emond, A. M. (2014). Sleep patterns in children with autistic spectrum disorders: A prospective cohort study. *Archives of Disease in Childhood*. https://doi.org/10.1136/archdischild-2013-304083
Hundley, R. J., Shui, A., & Malow, B. A. (2016). Relationship Between Subtypes of Restricted and Repetitive Behaviors and Sleep Disturbance in Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-016-2884-4
Huntley, J. D., Hampshire, A., Bor, D., Owen, A., & Howard, R. J. (2017). Adaptive working memory strategy training in early Alzheimer's disease: Randomised controlled trial. *British Journal of Psychiatry*. https://doi.org/10.1192/bjp.bp.116.182048
Hutson, J. R., Magri, R., Gareri, J. N., & Koren, G. (2010). The incidence of prenatal alcohol exposure in Montevideo Uruguay as determined by meconium analysis. *Therapeutic Drug Monitoring*, *32*(3), 311–317. https://doi.org/10.1097/FTD.0b013e3181dda52a
Inkelis, S. M., & Thomas, J. D. (2018). Sleep in Infants and Children with Prenatal Alcohol Exposure. *Alcoholism: Clinical and Experimental Research*, *42*(8), 1390–1405. https://doi.org/10.1111/acer.13803
Jan, J., Asante, K., Conry, J., Fast, D., Bax, M., Ipsiroglu, O., … Wasdell, M. (2010). Sleep health issues for children with FASD: clinical considerations. *International Journal of Pediatrics*, *2010*, 1–7. https://doi.org/10.1155/2010/639048
Jenni, O., & Carskadon, M. (2012). Sleep behavior and sleep regulation from infancy through adolescence: Normative aspects. *Sleep Medicine Clinics*. https://doi.org/10.1016/j.jsmc.2012.06.002
Jenni, O. G. (2005). Children's Sleep: An Interplay Between Culture and Biology. *PEDIATRICS*, *115*(1), 204–216. https://doi.org/10.1542/peds.2004-0815B
Jones, E. J. H., Gliga, T., Bedford, R., Charman, T., & Johnson, M. H. (2014). Developmental pathways to autism: A review of prospective studies of infants at risk. *Neuroscience and Biobehavioral Reviews*. https://doi.org/10.1016/j.neubiorev.2013.12.001
Jones, K. L., & Smith, D. W. (1973). Recognition of the fetal alcohol syndrome in early infancy. *Lancet*, *302*(7836), 999–1001. https://doi.org/10.1016/S0140-6736(73)91092-1
Jones, K., Smith, D., Ulleland, C., & Streissguth, A. (1973). Pattern of malformation of offspring in offspring of alcoholiic mothers. *The Lancet*, *301*(7815), 1267–1271. https://doi.org/10.1016/S0140-6736(73)91291-9
Kahn, A., Dan, B., Groswasser, J., Franco, P., & Sottiaux, M. (1996). Normal sleep architecture in infants and children. *Journal of Clinical Neurophysiology*. https://doi.org/10.1097/00004691-199605000-00002
Kahn, M., Fridenson, S., Lerer, R., Bar-Haim, Y., & Sadeh, A. (2014). Effects of one night of induced night-wakings versus sleep restriction on sustained attention and mood: A pilot study. *Sleep Medicine*. https://doi.org/10.1016/j.sleep.2014.03.016
Kamara, D., & Beauchaine, T. P. (2019). A Review of Sleep Disturbances among Infants and Children with Neurodevelopmental Disorders. *Review Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s40489-019-00193-8
Kambeitz, C., Klug, M. G., Greenmyer, J., Popova, S., & Burd, L. (2019). Association of adverse childhood experiences and neurodevelopmental disorders in people with fetal alcohol spectrum disorders (FASD) and non-FASD controls. *BMC Pediatrics*. https://doi.org/10.1186/s12887-019-1878-8
Kanner, L. (1943). Autistic disturbances of affective contact. *Nervous Child*. https://doi.org/10.1111/fwb.12896
Karbach, J., & Unger, K. (2014). Executive control training from middle childhood to adolescence. *Frontiers in Psychology*. https://doi.org/10.3389/fpsyg.2014.00390
Karmiloff-Smith, A. (2009). Nativism Versus Neuroconstructivism: Rethinking the Study of Developmental Disorders. *Developmental Psychology*. https://doi.org/10.1037/a0014506
Kashiwagi, M., & Hayashi, Y. (2016). The function of REM sleep: Implications from transgenic mouse models. *Brain and Nerve*.
Kaskie, R. E., Graziano, B., & Ferrarelli, F. (2017). Schizophrenia and sleep disorders: Links, risks, and management challenges. *Nature and Science of Sleep*. https://doi.org/10.2147/NSS.S121076
Keehn, B., Wagner, J., Tager-Flusberg, H., & Nelson, C. A. (2013). Functional connectivity in the first year of life in infants at-risk for autism: A preliminary near-infrared spectroscopy study. *Frontiers in Human Neuroscience*. https://doi.org/10.3389/fnhum.2013.00444
Keen, D., Adams, D., Simpson, K., den Houting, J., & Roberts, J. (2019). Anxiety-related symptomatology in young children on the autism spectrum. *Autism*. https://doi.org/10.1177/1362361317734692
Keiver, Bertram, Orr, P., Ipsiroglu, Khaleel, Gaetz, & Reynolds. (2013). Sleep disturbances in children with fetal alcohol spectrum disorder (fasd). *Alcoholism: Clinical and Experimental Research*, Vol. 37, p. 104A. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed11&NEWS=N&AN=71068215
Kelly, Y., Kelly, J., & Sacker, A. (2013). Time for bed: Associations with cognitive performance in 7-year-old children: A

longitudinal population-based study. *Journal of Epidemiology and Community Health*. https://doi.org/10.1136/jech-2012-202024
Kelly, Y., Zilanawala, A., Booker, C., & Sacker, A. (2018). Social Media Use and Adolescent Mental Health: Findings From the UK Millennium Cohort Study. *EClinicalMedicine*. https://doi.org/10.1016/j.eclinm.2018.12.005
Kerns, C. M., & Kendall, P. C. (2012). The Presentation and Classification of Anxiety in Autism Spectrum Disorder. *Clinical Psychology: Science and Practice*. https://doi.org/10.1111/cpsp.12009
Khonsary, S. (2017). THE BRAIN, an introduction to functional neuroanatomy. *Surgical Neurology International*. https://doi.org/10.4103/sni.sni_47_17
Khoury, J. E., Milligan, K., & Girard, T. A. (2015). Executive Functioning in Children and Adolescents Prenatally Exposed to Alcohol: A Meta-Analytic Review. *Neuropsychology Review*. https://doi.org/10.1007/s11065-015-9289-6
Kim, Y. K. (2019). Panic disorder: Current research and management approaches. *Psychiatry Investigation*. https://doi.org/10.30773/pi.2019.01.08
Kingdon, D., Cardoso, C., & McGrath, J. J. (2016). Research Review: Executive function deficits in fetal alcohol spectrum disorders and attention-deficit/hyperactivity disorder - a meta-analysis. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *57*(2), 116–131. https://doi.org/10.1111/jcpp.12451
Kitchin, E. (2009). The use of social stories to help bedtime resistance in a sample of young school-aged children.
Klinzing, J. G., Kugler, S., Soekadar, S. R., Rasch, B., Born, J., & Diekelmann, S. (2018). Odor cueing during slow-wave sleep benefits memory independently of low cholinergic tone. *Psychopharmacology*. https://doi.org/10.1007/s00213-017-4768-5
Klinzing, J. G., Rasch, B., Born, J., & Diekelmann, S. (2016). Sleep's role in the reconsolidation of declarative memories. *Neurobiology of Learning and Memory*. https://doi.org/10.1016/j.nlm.2016.10.004
Kluwe-Schiavon, B., Viola, T. W., Sanvicente-Vieira, B., Malloy-Diniz, L. F., & Grassi-Oliveira, R. (2017). Balancing automatic-controlled behaviors and emotional-salience states: A dynamic executive functioning hypothesis. *Frontiers in Psychology*. https://doi.org/10.3389/fpsyg.2016.02067
Kocevska, D., Muetzel, R. L., Luik, A. I., Luijk, M., Jaddoe, V. W., Verhulst, F. C., … Tiemeier, H. (2017). The Developmental Course of Sleep Disturbances Across Childhood Relates to Brain Morphology at Age 7: The Generation R Study. *Sleep*, *40*(1). https://doi.org/10.1093/sleep/zsw022
Kodituwakku, P., Coriale, G., Fiorentino, D., Aragon, A. S., Kalberg, W. O., Buckley, D., … May, P. A. (2006). Neurobehavioral characteristics of children with fetal alcohol spectrum disorders in communities from Italy: Preliminary results. *Alcoholism: Clinical and Experimental Research*, *30*(9), 1551–1561. https://doi.org/10.1111/j.1530-0277.2006.00187.x
Kodituwakku, P. W. (2009). Neurocognitive profile in children with fetal alcohol spectrum disorders. *Developmental Disabilities Research Reviews*, *15*(3), 218–224. https://doi.org/10.1002/ddrr.73; 10.1002/ddrr.73
Kooistra, L., Crawford, S., Gibbard, B., Kaplan, B. J., & Fan, J. (2011). Comparing attentional networks in fetal alcohol spectrum disorder and the inattentive and combined subtypes of attention deficit hyperactivity disorder. *Developmental Neuropsychology*. https://doi.org/10.1080/87565641.2010.549978
Krause, A. J., Simon, E. Ben, Mander, B. A., Greer, S. M., Saletin, J. M., Goldstein-Piekarski, A. N., & Walker, M. P. (2017). The sleep-deprived human brain. *Nature Reviews Neuroscience*. https://doi.org/10.1038/nrn.2017.55
Kronk, R., Bishop, E. E., Raspa, M., Bickel, J. O., Mandel, D. A., & Bailey, D. B. (2010). Prevalence, nature, and correlates of sleep problems among children with fragile X syndrome based on a large scale parent survey. *Sleep*. https://doi.org/10.1093/sleep/33.5.679
Kropotov, J. D. (2009). Quantitative EEG, Event-Related Potentials and Neurotherapy. In *Quantitative EEG, Event-Related Potentials and Neurotherapy*. https://doi.org/10.1016/B978-0-12-374512-5.X0001-1
Kryger, M. H., Dement, W. C., & Roth, T. (2010). Principles and practice of sleep medicine. In *Principles and Practice of Sleep Medicine, 5th Edition*. https://doi.org/10.1016/C2009-0-59875-3
Kuriyama, K., Mishima, K., Suzuki, H., Aritake, S., & Uchiyama, M. (2008). Sleep accelerates the improvement in working memory performance. *Journal of Neuroscience*. https://doi.org/10.1523/JNEUROSCI.2039-08.2008
Kuula, L., Pesonen, A.-K., Martikainen, S., Kajantie, E., Lahti, J., Strandberg, T., … Räikkönen, K. (2015). Poor sleep and neurocognitive function in early adolescence. *Sleep Medicine*, *16*(10), 1207–1212. https://doi.org/10.1016/j.sleep.2015.06.017
Lai, M. C., Lombardo, M. V., & Baron-Cohen, S. (2014). Autism. *The Lancet*. https://doi.org/10.1016/S0140-6736(13)61539-1
Lange, S., Rovet, J., Rehm, J., & Popova, S. (2017). Neurodevelopmental profile of Fetal Alcohol Spectrum Disorder: A systematic review. *BMC Psychology*, *5*(1), 1–12. https://doi.org/10.1186/s40359-017-0191-2
Lange, Shannon, Rehm, J., Anagnostou, E., & Popova, S. (2018). Prevalence of externalizing disorders and Autism Spectrum Disorders among children with Fetal Alcohol Spectrum Disorder: Systematic review and meta-analysis. *Biochemistry and Cell Biology*. https://doi.org/10.1139/bcb-2017-0014
Le Couteur, A. L., Gottesman, I., Bolton, P., Simonoff, E., Yuzda, E., Rutter, M., & Bailey, A. (1995). Autism as a strongly genetic disorder evidence from a british twin Study. *Psychological Medicine*. https://doi.org/10.1017/S0033291700028099
Lemoine, P., Harouseau, H., Borteryu, J. T., & Menuet, J. C. (1968). Les enfants des parents alcooliques: Anomalies observees apropos de 127 cas. *Ouest Medical*, *21*, 476 – 482.
Leonard, H. C., Bedford, R., Pickles, A., & Hill, E. L. (2015). Predicting the rate of language development from early motor

skills in at-risk infants who develop autism spectrum disorder. *Research in Autism Spectrum Disorders*. https://doi.org/10.1016/j.rasd.2014.12.012
Levin, A., & Scher, A. (2016). Sleep Problems in Young Children with Autism Spectrum Disorders: A Study of Parenting Stress, Mothers' Sleep-Related Cognitions, and Bedtime Behaviors. *CNS Neuroscience and Therapeutics*. https://doi.org/10.1111/cns.12651
Limoges, É., Bolduc, C., Berthiaume, C., Mottron, L., & Godbout, R. (2013). Relationship between poor sleep and daytime cognitive performance in young adults with autism. *Research in Developmental Disabilities*. https://doi.org/10.1016/j.ridd.2013.01.013
Lindgren, S., & Koeppl, G. (1987). Assessing child behavior problems in a medical setting: Development of the Pediatric Behavior Scale. *Advances in Behavioral Assessment of Children and Families*, *3*, 5790.
Lindor, E., Rinehart, N., & Fielding, J. (2018). Superior Visual Search and Crowding Abilities Are Not Characteristic of All Individuals on the Autism Spectrum. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-018-3601-2
Littner, M., Kushida, C., Anderson, W. M., Bailey, D., Berry, R. B., Davila, D. G., … Johnson, S. F. (2003). Practice parameters for the role of actigraphy in the study of sleep and circadian rhythms: an update for 2002. *Sleep*, *26*(3), 337–341.
Litwiller, B., Snyder, L. A., Taylor, W. D., & Steele, L. M. (2017). The relationship between sleep and work: A meta-analysis. *Journal of Applied Psychology*. https://doi.org/10.1037/apl0000169
Lo, J. C., Lee, S. M., Lee, X. K., Sasmita, K., Chee, N. I. Y. N., Tandi, J., … Chee, M. W. L. (2018). Sustained benefits of delaying school start time on adolescent sleep and well-being. *Sleep*. https://doi.org/10.1093/sleep/zsy052
Lombardo, M. V., Lai, M. C., & Baron-Cohen, S. (2019). Big data approaches to decomposing heterogeneity across the autism spectrum. *Molecular Psychiatry*. https://doi.org/10.1038/s41380-018-0321-0
Loomes, C., Rasmussen, C., Pei, J., Manji, S., & Andrew, G. (2008). The effect of rehearsal training on working memory span of children with fetal alcohol spectrum disorder. *Research in Developmental Disabilities*. https://doi.org/10.1016/j.ridd.2007.01.001
Loomis, A. L., Harvey, E. N., & Hobart, G. A. (1937). Cerebral states during sleep, as studied by human brain potentials. *Journal of Experimental Psychology*. https://doi.org/10.1037/h0057431
Lord, C., Rutter, M., DiLavore, P., Risi, S., Gotham, K., & Bishop, S. (2012). Autism Diagnostic Observation Schedule, Second Edition. *Torrance, CA: Western Psychological Services*.
Lord, C., Rutter, M., & Le Couteur, A. (1994). Autism Diagnostic Interview-Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/BF02172145
Lord, C., & Schopler, E. (1987). Neurobiological Implications of Sex Differences in Autism. In *Neurobiological Issues in Autism*. https://doi.org/10.1007/978-1-4899-1992-2_11
Lucas, B., Latimer, J., Doney, R., Watkins, R., Tsang, T., Hawkes, G., … Carter, M. (2016). Gross motor performance in children prenatally exposed to alcohol and living in remote Australia. *Journal of Paediatrics and Child Health*.
Lupton, C., Burd, L., & Harwood, R. (2004). Cost of fetal alcohol spectrum disorders. *American Journal of Medical Genetics. Part C, Seminars in Medical Genetics*, *127C*(1), 42–50. https://doi.org/10.1002/ajmg.c.30015
Lussier, A. A., Weinberg, J., & Kobor, M. S. (2017). Epigenetics studies of fetal alcohol spectrum disorder: Where are we now? *Epigenomics*. https://doi.org/10.2217/epi-2016-0163
MacNeil, B. M., Lopes, V. A., & Minnes, P. M. (2009). Anxiety in children and adolescents with Autism Spectrum Disorders. *Research in Autism Spectrum Disorders*. https://doi.org/10.1016/j.rasd.2008.06.001
Magiati, I., Ong, C., Lim, X. Y., Tan, J. W. L., Ong, A. Y. L., Patrycia, F., … Howlin, P. (2016). Anxiety symptoms in young people with autism spectrum disorder attending special schools: Associations with gender, adaptive functioning and autism symptomatology. *Autism*. https://doi.org/10.1177/1362361315577519
Maguire, E. A., Gadian, D. G., Johnsrude, I. S., Good, C. D., Ashburner, J., Frackowiak, R. S. J., & Frith, C. D. (2000). Navigation-related structural change in the hippocampi of taxi drivers. *Proceedings of the National Academy of Sciences of the United States of America*. https://doi.org/10.1073/pnas.070039597
Malow, B. A., Marzec, M. L., McGrew, S. G., Wang, L., Henderson, L. M., & Stone, W. L. (2006). Characterizing sleep in children with autism spectrum disorders: A multidimensional approach. *Sleep*. https://doi.org/10.1093/sleep/29.12.1563
Malow, B., Adkins, K. W., McGrew, S. G., Wang, L., Goldman, S. E., Fawkes, D., & Burnette, C. (2012). Melatonin for sleep in children with autism: A controlled trial examining dose, tolerability, and outcomes. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-011-1418-3
Mandy, W., & Tchanturia, K. (2015). Do women with eating disorders who have social and flexibility difficulties really have autism? A case series. *Molecular Autism*. https://doi.org/10.1186/2040-2392-6-6
Manly, T., Robertson, I. H., Galloway, M., & Hawkins, K. (1999). The absent mind: Further investigations of sustained attention to response. *Neuropsychologia*. https://doi.org/10.1016/S0028-3932(98)00127-4
Mannion, A., & Leader, G. (2014). Sleep Problems in Autism Spectrum Disorder: A Literature Review. *Review Journal of Autism and Developmental Disorders*, *1*(2), 101–109. https://doi.org/http://dx.doi.org/10.1007/s40489-013-0009-y
Marco, C. A., Wolfson, A. R., Sparling, M., & Azuaje, A. (2011). Family Socioeconomic Status and Sleep Patterns of Young Adolescents. *Behavioral Sleep Medicine*. https://doi.org/10.1080/15402002.2012.636298
Markovich, A. N., Gendron, M. A., & Corkum, P. V. (2015). Validating the Children's Sleep Habits Questionnaire against polysomnography and actigraphy in school-aged children. *Frontiers in Psychiatry*, *6*(JAN).

https://doi.org/10.3389/fpsyt.2014.00188
Marrone, M. (2014). *Attachment and interaction : from Bowlby to current clinical theory and practice.* Jessica Kingsley Publishers.
Martin, J. L., & Hakim, A. D. (2011). Wrist actigraphy. *Chest*, Vol. 139, pp. 1514–1527. https://doi.org/10.1378/chest.10-1872
Matlab, & Psychtools. (2020). Psychtoolbox-3. Retrieved April 8, 2020, from https://uk.mathworks.com/matlabcentral/fileexchange/70391-psychtoolbox-3
Mattson, S. N., Crocker, N., & Nguyen, T. T. (2011). Fetal alcohol spectrum disorders: Neuropsychological and behavioral features. *Neuropsychology Review*, Vol. 21, pp. 81–101. https://doi.org/10.1007/s11065-011-9167-9
Mattson, S. N., Foroud, T., Sowell, E. R., Jones, K. L., Coles, C. D., Fagerlund, Å., … Riley, E. P. (2010). Collaborative initiative on fetal alcohol spectrum disorders: Methodology of clinical projects. *Alcohol*, *44*(7–8), 635–641. https://doi.org/10.1016/j.alcohol.2009.08.005
May, P. A., Baete, A., Russo, J., Elliott, A. J., Blankenship, J., Kalberg, W. O., … Hoyme, H. E. (2014). Prevalence and characteristics of fetal alcohol spectrum disorders. *Pediatrics*, *134*(5), 855–866. https://doi.org/10.1542/peds.2013-3319
May, P. A., Chambers, C. D., Kalberg, W. O., Zellner, J., Feldman, H., Buckley, D., … Hoyme, H. E. (2018). Prevalence of fetal alcohol spectrum disorders in 4 US communities. *JAMA - Journal of the American Medical Association*. https://doi.org/10.1001/jama.2017.21896
May, P. A., Gossage, J. P., Kalberg, W. O., Robinson, L. K., Buckley, D., Manning, M., & Hoyme, H. E. (2009). Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in-school studies. *Developmental Disabilities Research Reviews*, Vol. 15, pp. 176–192. https://doi.org/10.1002/ddrr.68
May, T., Cornish, K., Conduit, R., Rajaratnam, S. M. W., & Rinehart, N. J. (2015). Sleep in High-Functioning Children With Autism: Longitudinal Developmental Change and Associations With Behavior Problems. *Behavioral Sleep Medicine*. https://doi.org/10.1080/15402002.2013.829064
Mayes, S. D., & Calhoun, S. L. (2009). Variables related to sleep problems in children with autism. *Research in Autism Spectrum Disorders*. https://doi.org/10.1016/j.rasd.2009.04.002
Mazefsky, C. A., Anderson, R., Conner, C. M., & Minshew, N. (2011). Child behavior checklist scores for school-aged children with autism: Preliminary evidence of patterns suggesting the need for referral. *Journal of Psychopathology and Behavioral Assessment*. https://doi.org/10.1007/s10862-010-9198-1
Mazzone, L., Postorino, V., Siracusano, M., Riccioni, A., & Curatolo, P. (2018). The Relationship between Sleep Problems, Neurobiological Alterations, Core Symptoms of Autism Spectrum Disorder, and Psychiatric Comorbidities. *Journal of Clinical Medicine*. https://doi.org/10.3390/jcm7050102
McLachlan, K., Rasmussen, C., Oberlander, T. F., Loock, C., Pei, J., Andrew, G., … Weinberg, J. (2016). Dysregulation of the cortisol diurnal rhythm following prenatal alcohol exposure and early life adversity. *Alcohol*. https://doi.org/10.1016/j.alcohol.2016.03.003
McQuire, C., Mukherjee, R., Hurt, L., Higgins, A., Greene, G., Farewell, D., … Paranjothy, S. (2019). Screening prevalence of fetal alcohol spectrum disorders in a region of the United Kingdom: A population-based birth-cohort study. *Preventive Medicine*, *118*, 344–351.
Meerlo, P., Mistlberger, R. E., Jacobs, B. L., Craig Heller, H., & McGinty, D. (2009). New neurons in the adult brain: The role of sleep and consequences of sleep loss. *Sleep Medicine Reviews*. https://doi.org/10.1016/j.smrv.2008.07.004
Meltzer, L. J., & McLaughlin Crabtree, V. (2015). Pediatric sleep problems: A clinician's guide to behavioral interventions. In *American Psychological Association*. https://doi.org/http://dx.doi.org/10.1037/14645-000
Meltzer, L. J., & Mindell, J. A. (2006). Sleep and Sleep Disorders in Children and Adolescents. *Psychiatric Clinics of North America*. https://doi.org/10.1016/j.psc.2006.08.004
Micheli, K., Komninos, I., Bagkeris, E., Roumeliotaki, T., Koutis, A., Kogevinas, M., & Chatzi, L. (2011). Sleep patterns in late pregnancy and risk of preterm birth and fetal growth restriction. *Epidemiology*. https://doi.org/10.1097/EDE.0b013e31822546fd
Mietchen, J. J., Bennett, D. P., Huff, T., Hedges, D. W., & Gale, S. D. (2016). Executive function in pediatric sleep-disordered breathing: A meta-analysis. *Journal of the International Neuropsychological Society*. https://doi.org/10.1017/S1355617716000643
Miles, J. H., Takahashi, T. N., Haber, A., & Hadden, L. (2003). Autism families with a high incidence of alcoholism. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1023/A:1025010828304
Mindell, J A, Boyle, J. T., Butler, R., Lipari, A., & Meltzer, L. J. (2014). Efficacy of behavioral interventions for pediatric insomnia. *Sleep*.
Mindell, Jodi A, & Owens, J. A. (2015). *A clinical guide to pediatric sleep : diagnosis and management of sleep problems* (Third edit; Judith A Owens, Ed.). Philadelphia : Wolters Kluwer.
Ming, X., Sun, Y.-M., Nachajon, R. V., Brimacombe, M., & Walters, A. S. (2009). Prevalence of Parasomnia in Autistic Children with Sleep Disorders. *Clinical Medicine. Pediatrics*. https://doi.org/10.4137/cmped.s1139
Morleo, M., Woolfall, K., Dedman, D., Mukherjee, R., Bellis, M. A., & Cook, P. A. (2011). Under-reporting of foetal alcohol spectrum disorders: an analysis of hospital episode statistics. *BMC Pediatrics*, *11*(1), 14. https://doi.org/10.1186/1471-2431-11-14
Morton, J., & Frith, U. (1995). Causal modeling: A structural approach to developmental psychopathology. *Developmental Psychopathology, Vol. 1: Theory and Methods.*

Moruzzi, G., & Magoun, H. W. (1949). Brain stem reticular formation and activation of the EEG. *Electroencephalography and Clinical Neurophysiology*. https://doi.org/10.1016/0013-4694(49)90219-9

Mottron, L., Dawson, M., Soulières, I., Hubert, B., & Burack, J. (2006). Enhanced perceptual functioning in autism: An update, and eight principles of autistic perception. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-005-0040-7

Mottron, L., Morasse, K., & Belleville, S. (2001). A study of memory functioning in individuals with autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. https://doi.org/10.1017/S0021963001006722

Mughal, R., & Dimitriou, D. (2017). Sleep, maladaptive behaviour and language acquisition in children with fetal alcohol spectrum disorders. *Sleep Medicine*. https://doi.org/10.1016/j.sleep.2017.11.675

Mughal, R., Joyce, A., Hill, C. M., & Dimitriou, D. (2020). Sleep Disturbance as a Predictor of Anxiety in Children With Fetal Alcohol Spectrum Disorders and Typically Developing Children. *Research in Developmental Disabilities*, *101*(103610). https://doi.org/https://doi.org/10.1016/j.ridd.2020.103610

Muhle, R. A., Reed, H. E., Stratigos, K. A., & Veenstra-VanderWeele, J. (2018). The emerging clinical neuroscience of autism spectrum disorder a review. *JAMA Psychiatry*. https://doi.org/10.1001/jamapsychiatry.2017.4685

Mukherjee, R, Layton, M., Yacoub, E., & Turk, J. (2011). Autism and autistic traits in people exposed to heavy prenatal alcohol: Data from a clinical series of 21 individuals and nested case control study. *Advances in Mental Health and Intellectual Disabilities*. https://doi.org/10.5042/amhid.2011.0015

Mukherjee, Raja. (2014). Diagnosis and Complexities. In B. Carpenter, C. Blackburn, & J. Egerton (Eds.), *Fetal Alcohol Spectrum Disorders, Interdisciplinary Perspectives* (p. 130). London: Routledge.

Mukherjee, Raja. (2019). FASD: the current situation in the UK. *Advances in Dual Diagnosis*. https://doi.org/10.1108/ADD-02-2019-040

Mukherjee, Raja, Wray, E., Commers, M., Hollins, S., & Curfs, L. (2013). The impact of raising a child with FASD upon carers: findings from a mixed methodology study in the UK. *Adoption and Fostering*. https://doi.org/10.1177/0308575913477331

Mulvaney, S. A., Goodwin, J. L., Morgan, W. J., Rosen, G. R., Quan, S. F., & Kaemingk, K. L. (2006). Behavior problems associated with sleep disordered breathing in school-aged children - The Tucson children's assessment of sleep apnea study. *Journal of Pediatric Psychology*. https://doi.org/10.1093/jpepsy/jsj035

Muratori, P., Menicucci, D., Lai, E., Battaglia, F., Bontempelli, L., Chericoni, N., & Gemignani, A. (2019). Linking Sleep to Externalizing Behavioral Difficulties: A Longitudinal Psychometric Survey in a Cohort of Italian School-Age Children. *Journal of Primary Prevention*. https://doi.org/10.1007/s10935-019-00547-2

Nash, K., Rovet, J., Greenbaum, R., Fantus, E., Nulman, I., & Koren, G. (2006). Identifying the behavioural phenotype in fetal alcohol spectrum disorder: Sensitivity, specificity and screening potential. *Archives of Women's Mental Health*, *9*(4), 181–186. https://doi.org/10.1007/s00737-006-0130-3

Nash, Kelly, Koren, G., & Rovet, J. (2011). A differential approach for examining the behavioural phenotype of fetal alcohol spectrum disorders. *J Popul Ther Clin Pharmacol*, *18*, e440-53. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21900707

National Autistic Society. (2020). The language we use to describe autism. Retrieved April 8, 2020, from https://www.autism.org.uk/about/what-is/describing.aspx

National Sleep Foundation. (2016). How Much Sleep Do We Really Need? *Sleep Research*. https://doi.org/10.1126/science.1178713

NHS England. (2012). Estimating the Prevalence of Autism Spectrum Conditions in Adults - Extending the 2007 Adult Psychiatric Morbidity Survey. Retrieved April 8, 2020, from https://digital.nhs.uk/data-and-information/publications/statistical/estimating-the-prevalence-of-autism-spectrum-conditions-in-adults/estimating-the-prevalence-of-autism-spectrum-conditions-in-adults-extending-the-2007-adult-psychiatric-morbidity-survey

NHS England, Brugha, T., Cooper, S., McManus, S., Purdon, S., Smith, J., … Tryer, F. (2012). Estimating the Prevalence of Autism Spectrum Conditions in Adults - Extending the 2007 Adult Psychiatric Morbidity Survey. Retrieved April 8, 2020, from The NHS Information Centre for Health and Social Care website: https://digital.nhs.uk/data-and-information/publications/statistical/estimating-the-prevalence-of-autism-spectrum-conditions-in-adults/estimating-the-prevalence-of-autism-spectrum-conditions-in-adults-extending-the-2007-adult-psychiatric-morbidity-survey

NHS Health Research Authority. (2020). Assessment of alcohol consumption in pregnancy. Retrieved from https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/assessment-of-alcohol-consumption-in-pregnancy/

Nickl-Jockschat, T., Habel, U., Maria Michel, T., Manning, J., Laird, A. R., Fox, P. T., … Eickhoff, S. B. (2012). Brain structure anomalies in autism spectrum disorder-a meta-analysis of VBM studies using anatomic likelihood estimation. *Human Brain Mapping*. https://doi.org/10.1002/hbm.21299

Nijhuis, J. G., Prechtl, H. F. R., Martin, C. B., & Bots, R. S. G. M. (1982). Are there behavioural states in the human fetus? *Early Human Development*. https://doi.org/10.1016/0378-3782(82)90106-2

Novick Brown, N., Connor, P. D., & Adler, R. S. (2012). Conduct-Disordered Adolescents With Fetal Alcohol Spectrum Disorder: Intervention in Secure Treatment Settings. *Criminal Justice and Behavior*, *39*, 770–793. https://doi.org/10.1177/0093854812437919

O'Connor, & Rutter. (2000). Attachment Disorder Behavior Following Early Severe Deprivation: Extension and Longitudinal Follow-up. *Journal of the American Academy of Child & Adolescent Psychiatry*, *39*(6), 703–712. https://doi.org/10.1097/00004583-200006000-00008

O'Riordan, M. A., Plaisted, K. C., Driver, J., & Baron-Cohen, S. (2001). Superior visual search in autism. *Journal of Experimental Psychology: Human Perception and Performance*. https://doi.org/10.1037/0096-1523.27.3.719

Office for National Statistics. (2016). The National Statistics Socio-economic classification (NS-SEC). Retrieved from https://www.ons.gov.uk/methodology/classificationsandstandards/otherclassifications/thenationalstatisticssocioeconomicclassificationnssecrebasedonsoc2010

Ooi, Y. P., Rescorla, L., Ang, R. P., Woo, B., & Fung, D. S. S. (2011). Identification of Autism Spectrum Disorders using the child behavior checklist in Singapore. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-010-1015-x

Owens, J A, Spirito, A., & McGuinn, M. (2000). The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children. *Sleep*, *23*(8), 1043–1051. https://doi.org/10.1111/j.1469-8749.2001.tb00204.x

Ozonoff, S., & Jensen, J. (1999). Specific executive function profiles in three neurodevelopmental disorders. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1023/A:1023052913110

Padmanabhan, A., Lynch, C. J., Schaer, M., & Menon, V. (2017). The Default Mode Network in Autism. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. https://doi.org/10.1016/j.bpsc.2017.04.004

Pagan, C., Goubran-Botros, H., Delorme, R., Benabou, M., Lemière, N., Murray, K., … Bourgeron, T. (2017). Disruption of melatonin synthesis is associated with impaired 14-3-3 and miR-451 levels in patients with autism spectrum disorders. *Scientific Reports*. https://doi.org/10.1038/s41598-017-02152-x

Palomo, R., Belinchón, M., & Ozonoff, S. (2006). Autism and family home movies: A comprehensive review. *Journal of Developmental and Behavioral Pediatrics*. https://doi.org/10.1097/00004703-200604002-00003

Paolozza, A., Rasmussen, C., Pei, J., Hanlon-Dearman, A., Nikkel, S. M., Andrew, G., … Reynolds, J. N. (2014). Working memory and visuospatial deficits correlate with oculomotor control in children with fetal alcohol spectrum disorder. *Behavioural Brain Research*. https://doi.org/10.1016/j.bbr.2014.01.024

Park, H. R., Lee, J. M., Moon, H. E., Lee, D. S., Kim, B. N., Kim, J., … Paek, S. H. (2016). A short review on the current understanding of autism spectrum disorders. *Experimental Neurobiology*. https://doi.org/10.5607/en.2016.25.1.1

Pattyn, N., Neyt, X., Henderickx, D., & Soetens, E. (2008). Psychophysiological investigation of vigilance decrement: Boredom or cognitive fatigue? *Physiology and Behavior*. https://doi.org/10.1016/j.physbeh.2007.09.016

Patzold, L. M., Richdale, A. L., & Tonge, B. J. (1998). An investigation into sleep characteristics of children with autism and Asperger's Disorder. *Journal of Paediatrics and Child Health*. https://doi.org/10.1046/j.1440-1754.1998.00291.x

Peadon, E. (2010). Distinguishing between attention-deficit hyperactivity and fetal alcohol spectrum disorders in children: clinical guidelines. *Neuropsychiatric Disease and Treatment*. https://doi.org/10.2147/ndt.s7256

Peadon, E., Fremantle, E., Bower, C., & Elliott, E. J. (2008). International survey of diagnostic services for children with Fetal Alcohol Spectrum Disorders. *BMC Pediatr*, *8*, 12. https://doi.org/1471-2431-8-12 [pii]\r10.1186/1471-2431-8-12

Pei, J., Denys, K., Hughes, J., & Rasmussen, C. (2011). Mental health issues in fetal alcohol spectrum disorder. *Journal of Mental Health*, *20*(5), 473–483. https://doi.org/10.3109/09638237.2011.577113

Pellicano, E. (2011). Psychological models of autism: An overview. In *Researching the Autism Spectrum: Contemporary Perspectives*. https://doi.org/10.1017/CBO9780511973918.010

Pichini, S., Busardò, F. P., Ceccanti, M., Tarani, L., Pacifici, R., & Italian Society on FASD (SIFASD). (2017). Unreliable estimation of prevalence of fetal alcohol syndrome. *The Lancet. Global Health*, *5*(6), e574. https://doi.org/10.1016/S2214-109X(17)30173-0

Popova, S., Lange, S., Burd, L., & Rehm, J. (2016). The economic burden of fetal alcohol spectrum disorder in Canada in 2013. *Alcohol and Alcoholism*. https://doi.org/10.1093/alcalc/agv117

Popova, S., Lange, S., Burd, L., Urbanoski, K., & Rehm, J. (2013). Cost of specialized addiction treatment of clients with fetal alcohol spectrum disorder in Canada. *BMC Public Health*. https://doi.org/10.1186/1471-2458-13-570

Popova, S., Lange, S., Probst, C., Gmel, G., & Rehm, J. (2017). Estimation of national, regional, and global prevalence of alcohol use during pregnancy and fetal alcohol syndrome: a systematic review and meta-analysis. *The Lancet Global Health*, *5*(3), e290–e299. https://doi.org/10.1016/S2214-109X(17)30021-9

Popova, S., Lange, S., Shield, K., Mihic, A., Chudley, A., Mukherjee, R., … Rehm, J. (2016). Comorbidity of fetal alcohol spectrum disorder: A systematic review and meta-analysis. *The Lancet*, *387*(10022), 978–987. https://doi.org/10.1016/S0140-6736(15)01345-8

Premack, D., & Woodruff, G. (1978). Does the chimpanzee have a theory of mind? *Behavioral and Brain Sciences*. https://doi.org/10.1017/S0140525X00076512

Price, A., Cook, P., Norgate, S., & Mukherjee, R. (2017). Prenatal alcohol exposure and traumatic childhood experiences: A systematic review. *Neuroscience & Biobehavioral Reviews*, *80*, 89–98. https://doi.org/10.1016/j.neubiorev.2017.05.018

Pring, L., Ryder, N., Crane, L., & Hermelin, B. (2012). Creativity in savant artists with autism. *Autism*. https://doi.org/10.1177/1362361311403783

Quach, J., Spencer-Smith, M., Anderson, P. J., & Roberts, G. (2018). Can working memory training improve children's sleep? *Sleep Medicine*. https://doi.org/10.1016/j.sleep.2017.11.1143

Randall, M., Egberts, K. J., Samtani, A., Scholten, R. J. P. M., Hooft, L., Livingstone, N., … Williams, K. (2018). Diagnostic tests for autism spectrum disorder (ASD) in preschool children. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD009044.pub2

Rangmar, J., Sandberg, A. D., Aronson, M., & Fahlke, C. (2015). Cognitive and executive functions, social cognition and

sense of coherence in adults with fetal alcohol syndrome. *Nordic Journal of Psychiatry*. https://doi.org/10.3109/08039488.2015.1009487
Rapee, R. M., Schniering, C. A., & Hudson, J. L. (2009). Anxiety Disorders During Childhood and Adolescence: Origins and Treatment. *Annual Review of Clinical Psychology*. https://doi.org/10.1146/annurev.clinpsy.032408.153628
Rasmussen, C. (2005). Executive functioning and working memory in fetal alcohol spectrum disorder. *Alcoholism: Clinical and Experimental Research*. https://doi.org/10.1097/01.alc.0000175040.91007.d0
Rasmussen, C., & Bisanz, J. (2011). The relation between mathematics and working memory in young children with fetal alcohol spectrum disorders. *Journal of Special Education*. https://doi.org/10.1177/0022466909356110
Rasmussen, C., Talwar, V., Loomes, C., & Andrew, G. (2008). Brief report: Lie-telling in children with fetal alcohol spectrum disorder. *Journal of Pediatric Psychology*. https://doi.org/10.1093/jpepsy/jsm069
Raven, J., Raven, J. C., & Court, J. (1998). Manual for Raven's progressive matrices and vocabulary scales. In *Raven manual*. Retrieved from http://books.google.es/books?id=YrvAAQAACAAJ
Remington, A., & Fairnie, J. (2017). A sound advantage: Increased auditory capacity in autism. *Cognition*. https://doi.org/10.1016/j.cognition.2017.04.002
Remington, A., Swettenham, J., Campbell, R., & Coleman, M. (2009). Selective attention and perceptual load in autism spectrum disorder. *Psychological Science*. https://doi.org/10.1111/j.1467-9280.2009.02454.x
Reynaud, E., Vecchierini, M. F., Heude, B., Charles, M. A., & Plancoulaine, S. (2018). Sleep and its relation to cognition and behaviour in preschool-aged children of the general population: a systematic review. *Journal of Sleep Research*. https://doi.org/10.1111/jsr.12636
Rinehart, N. J., Bradshaw, J. L., Brereton, A. V., & Tonge, B. J. (2001). Movement Preparation in High-Functioning Autism and Asperger Disorder: A Serial Choice Reaction Time Task Involving Motor Reprogramming. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1023/A:1005617831035
Rinehart, N. J., Bradshaw, J. L., Moss, S. A., Brereton, A. V., & Tonge, B. J. (2001). A deficit in shifting attention present in high-functioning autism but not Asperger's disorder. *Autism*. https://doi.org/10.1177/1362361301005001007
Roebuck-Spencer, T. M., Mattson, S. N., Marion, S. D., Brown, W. S., & Riley, E. P. (2004). Bimanual coordination in alcohol-exposed children: Role of the corpus callosum. *Journal of the International Neuropsychological Society*. https://doi.org/10.1017/S1355617704104116
Roth, R. M., Isquith, P. K., & Gioia, G. A. (2014). Assessment of executive functioning using the behavior rating inventory of executive function (BRIEF). In *Handbook of Executive Functioning*. https://doi.org/10.1007/978-1-4614-8106-5_18
Rutter, M. (2005). Incidence of autism spectrum disorders: Changes over time and their meaning. *Acta Paediatrica, International Journal of Paediatrics*. https://doi.org/10.1080/08035250410023124
Rzepecka, H., Mckenzie, K., McClure, I., & Murphy, S. (2011). Sleep, anxiety and challenging behaviour in children with intellectual disability and/or autism spectrum disorder. *Research in Developmental Disabilities*. https://doi.org/10.1016/j.ridd.2011.05.034
Sadeh, A., Gruber, R., & Raviv, A. (2002). Sleep, Neurobehavioral Functioning, and Behavior Problems in School-Age Children. *Child Development*, *73*(2), 405–417. https://doi.org/10.1111/1467-8624.00414
Sadeh, A., Gruber, R., & Raviv, A. (2003). The Effects of Sleep Restriction and Extension on School-Age Children: What a Difference an Hour Makes. *Child Development*. https://doi.org/10.1111/1467-8624.7402008
Sakata-Haga, H., Dominguez, H. D., Sei, H., Fukui, Y., Riley, E. P., & Thomas, J. D. (2006). Alterations in circadian rhythm phase shifting ability in rats following ethanol exposure during the third trimester brain growth spurt. *Alcoholism: Clinical and Experimental Research*, *30*(5), 899–907. https://doi.org/10.1111/j.1530-0277.2006.00105.x
Salomone, E., Charman, T., Mcconachie, H., & Warreyn, P. (2016). Child's verbal ability and gender are associated with age at diagnosis in a sample of young children with ASD in Europe. *Child: Care, Health and Development*. https://doi.org/10.1111/cch.12261
Sarchiapone, M., Mandelli, L., Carli, V., Iosue, M., Wasserman, C., Hadlaczky, G., … Wasserman, D. (2014). Hours of sleep in adolescents and its association with anxiety, emotional concerns, and suicidal ideation. *Sleep Medicine*. https://doi.org/10.1016/j.sleep.2013.11.780
Schauder, K. B., Mash, L. E., Bryant, L. K., & Cascio, C. J. (2015). Interoceptive ability and body awareness in autism spectrum disorder. *Journal of Experimental Child Psychology*. https://doi.org/10.1016/j.jecp.2014.11.002
Schonfeld, A. M., Mattson, S. N., & Riley, E. P. (2005). Moral maturity and delinquency after prenatal alcohol exposure. *Journal of Studies on Alcohol*. https://doi.org/10.15288/jsa.2005.66.545
Schonfeld, A. M., Paley, B., Frankel, F., & O'Connor, M. J. (2006). Executive functioning predicts social skills following prenatal alcohol exposure. *Child Neuropsychology : A Journal on Normal and Abnormal Development in Childhood and Adolescence*, *12*(310), 439–452. https://doi.org/10.1080/09297040600611338
Schreck, K. A., Mulick, J. A., & Smith, A. F. (2004). Sleep problems as possible predictors of intensified symptoms of autism. *Research in Developmental Disabilities*. https://doi.org/10.1016/j.ridd.2003.04.007
Schweppe, J., & Rummer, R. (2014). Attention, Working Memory, and Long-Term Memory in Multimedia Learning: An Integrated Perspective Based on Process Models of Working Memory. *Educational Psychology Review*. https://doi.org/10.1007/s10648-013-9242-2
Scott, F. J. (2013). The development of imagination in children with autism. In *The Oxford Handbook of the Development of Imagination*. https://doi.org/10.1093/oxfordhb/9780195395761.013.0032
Seligman, L. D., Swedish, E. F., & Flannery-Schroeder, E. (2014). *Anxiety Assessment and Treatment in Typically Developing Children*. https://doi.org/10.1007/978-3-319-06796-4_5

Senju, A., Southgate, V., White, S., & Frith, U. (2009). Mindblind eyes: An absence of spontaneous theory of mind in Asperger syndrome. *Science*. https://doi.org/10.1126/science.1176170

Serdarevic, F., Tiemeier, H., Jansen, P. R., Alemany, S., Xerxa, Y., Neumann, A., … Ghassabian, A. (2020). Polygenic Risk Scores for Developmental Disorders, Neuromotor Functioning During Infancy, and Autistic Traits in Childhood. *Biological Psychiatry*. https://doi.org/10.1016/j.biopsych.2019.06.006

Sergeant, J. A., Geurts, H., & Oosterlaan, J. (2002). How specific is a deficit of executive functioning for attention-deficit/hyperactivity disorder? *Behavioural Brain Research*. https://doi.org/10.1016/S0166-4328(01)00430-2

Shah, A., & Frith, U. (1993). Why Do Autistic Individuals Show Superior Performance on the Block Design Task? *Journal of Child Psychology and Psychiatry*. https://doi.org/10.1111/j.1469-7610.1993.tb02095.x

Shang, C. Y., Gau, S. S. F., & Soong, W. T. (2006). Association between childhood sleep problems and perinatal factors, parental mental distress and behavioral problems. *Journal of Sleep Research*, *15*(1), 63–73. https://doi.org/10.1111/j.1365-2869.2006.00492.x

Shattuck, P. T. (2006). The contribution of diagnostic substitution to the growing administrative prevalence of autism in US special education. *Pediatrics*. https://doi.org/10.1542/peds.2005-1516

Shirama, A., Kato, N., & Kashino, M. (2017). When do individuals with autism spectrum disorder show superiority in visual search? *Autism*. https://doi.org/10.1177/1362361316656943

Short, M. A., Blunden, S., Rigney, G., Matricciani, L., Coussens, S., M. Reynolds, C., & Galland, B. (2018). Cognition and objectively measured sleep duration in children: a systematic review and meta-analysis. *Sleep Health*. https://doi.org/10.1016/j.sleh.2018.02.004

Sikora, D. M., Johnson, K., Clemons, T., & Katz, T. (2012). The relationship between sleep problems and daytime behavior in children of different ages with autism spectrum disorders. *Pediatrics*. https://doi.org/10.1542/peds.2012-0900F

Simard, I., Luck, D., Mottron, L., Zeffiro, T. A., & Soulières, I. (2015). Autistic fluid intelligence: Increased reliance on visual functional connectivity with diminished modulation of coupling by task difficulty. *NeuroImage: Clinical*. https://doi.org/10.1016/j.nicl.2015.09.007

Simmons, R. W., Wass, T., Thomas, J. D., & Riley, E. P. (2002). Fractionated simple and choice reaction time in children with prenatal exposure to alcohol. *Alcoholism: Clinical and Experimental Research*. https://doi.org/10.1097/00000374-200209000-00015

Smith, M. T., McCrae, C. S., Cheung, J., Martin, J. L., Harrod, C. G., Heald, J. L., & Carden, K. A. (2018). Use of Actigraphy for the Evaluation of Sleep Disorders and Circadian Rhythm Sleep-Wake Disorders: An American Academy of Sleep Medicine Systematic Review, Meta-Analysis, and GRADE Assessment. *Journal of Clinical Sleep Medicine*. https://doi.org/10.5664/jcsm.7228

Soh, D. W., Skocic, J., Nash, K., Stevens, S., Turner, G. R., & Rovet, J. (2015). Self-Regulation therapy increases frontal gray matter in children with fetal alcohol spectrum disorder: Evaluation by Voxel-Based morphometry. *Frontiers in Human Neuroscience*. https://doi.org/10.3389/fnhum.2015.00108

Soulieres, I., & Mottron, L. (2013). Rethinking education for autistic children based on their cognitive strengths and learning mechanisms. *Frontiers in Human Neuroscience*.

Spence, S. (1998). A measure of anxiety symptoms among children. *Behaviour Research and Therapy*, *36*(5), 545–566. https://doi.org/10.1016/S0005-7967(98)00034-5

Spence, S. H. (1997). Structure of anxiety symptoms among children: a confirmatory factor-analytic study. *Journal of Abnormal Psychology*, *106*(2), 280–297. https://doi.org/10.1037/0021-843X.106.2.280

Spezio, M. L., Adolphs, R., Hurley, R. S. E., & Piven, J. (2007). Abnormal use of facial information in high-functioning autism. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-006-0232-9

Spruyt, K., & Gozal, D. (2011a). Pediatric sleep questionnaires as diagnostic or epidemiological tools: A review of currently available instruments. *Sleep Medicine Reviews*, Vol. 15, pp. 19–32. https://doi.org/10.1016/j.smrv.2010.07.005

Spruyt, K., & Gozal, D. (2011b). Sleep disturbances in children with attention-deficit/hyperactivity disorder. *Expert Review of Neurotherapeutics*, *11*(4), 565–577. https://doi.org/10.1586/ern.11.7

Spruyt, K., Ipsiroglu, O., Stockler, S., & Reynolds, J. N. (2018). Challenging sleep-wake behaviors reported in informal, conversational interviews of caregivers of children with fetal alcohol spectrum disorder. *International Journal of Developmental Disabilities*, *64*(2), 65–74. https://doi.org/10.1080/20473869.2016.1229395

Stade, Barozzino, Bennett, Jeffs, Laird, Patterson, … Stephens. (2010). The nature of sleep in canadian children with fetal alcohol spectrum disorder. *Paediatrics and Child Health*, Vol. 15, p. 51A. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed12&NEWS=N&AN=70780325

Staner, L. (2010). Comorbidity of insomnia and depression. *Sleep Medicine Reviews*. https://doi.org/10.1016/j.smrv.2009.09.003

Steinhausen, H. C., & Spohr, H. L. (1998). Long-term outcome of children with fetal alcohol syndrome: psychopathology, behavior, and intelligence. *Alcohol Clin Exp Res*, *22*(2), 334–338. https://doi.org/10.1111/j.1530-0277.1998.tb03657.x

Stern, E. R., Goodman, W. K., Taylor, S. F., Abelson, J. L., Goodman, W. K., & Muratore, A. F. (2017). Switching between internally and externally focused attention in obsessive-compulsive disorder: Abnormal visual cortex activation and connectivity. *Psychiatry Research - Neuroimaging*. https://doi.org/10.1016/j.pscychresns.2016.08.006

Stevens, S., Nash, K., Koren, G., & Rovet, J. (2013). Autism characteristics in children with fetal alcohol spectrum disorders. *Child Neuropsychology : A Journal on Normal and Abnormal Development in Childhood and Adolescence*, *19*(6), 579–587. https://doi.org/10.1080/09297049.2012.727791

Stone, W. S., Altman, H. J., Hall, J., Arankowsky-Sandoval, G., Parekh, P., & Gold, P. E. (1996). Prenatal exposure to alcohol in adult rats: Relationships between sleep and memory deficits, and effects of glucose administration on memory. *Brain Research*, *742*(1–2), 98–106. https://doi.org/10.1016/S0006-8993(96)00976-6

Streissguth, A., Bookstein, F. L., Barr, H. M., Press, S., & Sampson, P. D. (1998). A fetal alcohol behavior scale. *Alcoholism, Clinical and Experimental Research*, *22*(2), 325–333. https://doi.org/10.1111/j.1530-0277.1998.tb03656.x

Streissguth, A. P., Bookstein, F. L., Barr, H. M., Sampson, P. D., O'Malley, K., & Young, J. K. (2004). Risk factors for adverse life outcomes in fetal alcohol syndrome and fetal alcohol effects. *Journal of Developmental and Behavioral Pediatrics*, *25*(4), 228–238. https://doi.org/10.1097/00004703-200408000-00002

Streissguth, Barr, Kogan, & Bookstein. (1996). Understanding the Ocurrence of Secondary Disabilities in Clients with Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE). *Centers for Disease Control and Prevention*.

Sung, J. E. (2011). The Reliability and Validity of Short-term and Working Memory Pointing Tasks Developed for Clinical Populations with Speech and Language Disorders. *Commun Sci Disord*, *16*(2), 185–201. Retrieved from http://www.e-csd.org/journal/view.php?number=459

Sung, V., Hiscock, H., & Sciberras, E. (2008). Sleep Problems in Children With Attention-Deficit/Hyperactivity Disorder Prevalence and the Effect on the Child and Family. *Archives of Pediatrics & Adolescent Medicine*, *162*(4), 336–342. https://doi.org/10.1001/archpedi.162.4.336

Surtees, A. D. R., Oliver, C., Jones, C. A., Evans, D. L., & Richards, C. (2018). Sleep duration and sleep quality in people with and without intellectual disability: A meta-analysis. *Sleep Medicine Reviews*. https://doi.org/10.1016/j.smrv.2017.11.003

Tabernero, C., Figols, J., Cuadrado, N., Claveria, L. E., Polo, J. M., Sevillano, M. D., … Carpizo, R. (2000). Fatal familial insomnia: Clinical, neuropathological, and genetic description of a Spanish family. *Journal of Neurology Neurosurgery and Psychiatry*. https://doi.org/10.1136/jnnp.68.6.774

Tager-Flusberg, H., & Kasari, C. (2013). Minimally verbal school-aged children with autism spectrum disorder: The neglected end of the spectrum. *Autism Research*. https://doi.org/10.1002/aur.1329

Taylor, D. C., Neville, B. G. R., & Cross, J. H. (1999). Autistic spectrum disorders in childhood epilepsy surgery candidates. *European Child and Adolescent Psychiatry*. https://doi.org/10.1007/s007870050128

Tegelbeckers, J., Bunzeck, N., Duzel, E., Bonath, B., Flechtner, H. H., & Krauel, K. (2015). Altered salience processing in attention deficit hyperactivity disorder. *Human Brain Mapping*. https://doi.org/10.1002/hbm.22755

Teh, E. J., Chan, D. M. E., Tan, G. K. J., & Magiati, I. (2017). Continuity and Change in, and Child Predictors of, Caregiver Reported Anxiety Symptoms in Young People with Autism Spectrum Disorder: A Follow-Up Study. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-017-3136-y

Thanh, N. X., Jonsson, E., Moffatt, J., & Dennett, L. (2013). Fetal alcohol spectrum disorder--poverty trap? *Journal of Population Therapeutics and Clinical Pharmacology = Journal de La Therapeutique Des Populations et de La Pharmacologie Clinique*, *20*(1). https://doi.org/10.1001/jama.290.22.2996

Tick, B., Bolton, P., Happé, F., Rutter, M., & Rijsdijk, F. (2016). Heritability of autism spectrum disorders: A meta-analysis of twin studies. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. https://doi.org/10.1111/jcpp.12499

Tietze, A. L., Blankenburg, M., Hechler, T., Michel, E., Koh, M., Schlüter, B., & Zernikow, B. (2012). Sleep disturbances in children with multiple disabilities. *Sleep Medicine Reviews*. https://doi.org/10.1016/j.smrv.2011.03.006

Tordjman, S., Anderson, G. M., Pichard, N., Charbuy, H., & Touitou, Y. (2005). Nocturnal excretion of 6-sulphatoxymelatonin in children and adolescents with autistic disorder. *Biological Psychiatry*. https://doi.org/10.1016/j.biopsych.2004.11.003

Torres, E. B., & Denisova, K. (2016). Motor noise is rich signal in autism research and pharmacological treatments. *Scientific Reports*. https://doi.org/10.1038/srep37422

Touchette, E., Petit, D., Séguin, J. R., Boivin, M., Tremblay, R. E., & Montplaisir, J. Y. (2007). Associations between sleep duration patterns and behavioral/cognitive functioning at school entry. *Sleep*. https://doi.org/10.1093/sleep/30.9.1213

Trejos-Castillo, E., & Trevino-Schafer, N. (2018). Handbook of foster youth. In *Handbook of Foster Youth*. https://doi.org/10.4324/9781351168243

Tsai, T.-H., Chen, Y.-L., & Gau, S. S.-F. (2019). Relationships between autistic traits, insufficient sleep, and real-world executive functions in children: a mediation analysis of a national epidemiological survey. *Psychological Medicine*. https://doi.org/10.1017/s0033291719003271

Tucker, M. A., Humiston, G. B., Summer, T., & Wamsley, E. (2020). Comparing the effects of sleep and rest on memory consolidation. *Nature and Science of Sleep*. https://doi.org/10.2147/NSS.S223917

Turnbull, K., Reid, G. J., & Morton, J. B. (2013). Behavioral Sleep Problems and their Potential Impact on Developing Executive Function in Children. *Sleep*. https://doi.org/10.5665/sleep.2814

UK Department for Education. (2019). Special educational needs in England: January 2019. Retrieved April 8, 2020, from https://www.gov.uk/government/statistics/special-educational-needs-in-england-january-2019

Ulleland, C. N. (1972). The offspring of alcoholic mothers. *Annals of the New York Academy of Sciences*, *197*(1), 167–169. https://doi.org/10.1111/j.1749-6632.1972.tb28142.x

Urbain, C., De Tiège, X., Op De Beeck, M., Bourguignon, M., Wens, V., Verheulpen, D., … Peigneux, P. (2016). Sleep in children triggers rapid reorganization of memory-related brain processes. *NeuroImage*. https://doi.org/10.1016/j.neuroimage.2016.03.055

Verhoeff, M. E., Blanken, L. M. E., Kocevska, D., Mileva-Seitz, V. R., Jaddoe, V. W. V., White, T., … Tiemeier, H. (2018). The

bidirectional association between sleep problems and autism spectrum disorder: A population-based cohort study. *Molecular Autism*. https://doi.org/10.1186/s13229-018-0194-8

Vermeulen, M. C. M., Van der Heijden, K. B., Swaab, H., & Van Someren, E. J. W. (2019). Sleep spindle characteristics and sleep architecture are associated with learning of executive functions in school-age children. *Journal of Sleep Research*. https://doi.org/10.1111/jsr.12779

Walters, A. S., Silvestri, R., Zucconi, M., Chandrashekariah, R., & Konofal, E. (2008). Review of the possible relationship and hypothetical links between Attention Deficit Hyperactivity Disorder (ADHD) and the simple sleep related movement disorders, parasomnias, hypersomnias, and circadian rhythm disorders. *Journal of Clinical Sleep Medicine*. https://doi.org/10.5664/jcsm.27356

Wass, S. V., Jones, E. J. H., Gliga, T., Smith, T. J., Charman, T., Johnson, M. H., … Volein, A. (2015). Shorter spontaneous fixation durations in infants with later emerging autism. *Scientific Reports*. https://doi.org/10.1038/srep08284

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology*. https://doi.org/10.1037//0022-3514.54.6.1063

Wechsler, D. (1997). Wechsler adult intelligence scale - Third Edition (WAIS-III). *San Antonio*.

Weiskop, S., Richdale, A., & Matthews, J. (2005). Behavioural treatment to reduce sleep problems in children with autism or fragile X syndrome. *Developmental Medicine and Child Neurology*. https://doi.org/10.1017/S0012162205000186

Wenar, C., & Kerig, P. (2000). Developmental psychopathology: From infancy through adolescence. In *Developmental psychopathology: From infancy through adolescence (4th ed.)*.

Wengel, T., Hanlon-Dearman, A. C., & Fjeldsted, B. (2011a). Sleep and sensory characteristics in young children with fetal alcohol spectrum disorder. *Journal of Developmental and Behavioral Pediatrics*, *32*(5), 384–392. https://doi.org/10.1097/DBP.0b013e3182199694

Wengel, T., Hanlon-Dearman, A. C., & Fjeldsted, B. (2011b). Sleep and sensory characteristics in young children with fetal alcohol spectrum disorder. *Journal of Developmental and Behavioral Pediatrics*, *32*(5), 384–392. https://doi.org/10.1097/DBP.0b013e3182199694

Werling, D. M., & Geschwind, D. H. (2013). Sex differences in autism spectrum disorders. *Current Opinion in Neurology*. https://doi.org/10.1097/WCO.0b013e32835ee548

Wheelwright, S., Auyeung, B., Allison, C., & Baron-Cohen, S. (2010). Defining the broader, medium and narrow autism phenotype among parents using the Autism Spectrum Quotient (AQ). *Molecular Autism*. https://doi.org/10.1186/2040-2392-1-10

Whitney, P., Hinson, J. M., & Nusbaum, A. T. (2019). A dynamic attentional control framework for understanding sleep deprivation effects on cognition. In *Progress in Brain Research*. https://doi.org/10.1016/bs.pbr.2019.03.015

Wieczorek, L., Fish, E. W., O'Leary-Moore, S. K., Parnell, S. E., & Sulik, K. K. (2015). Hypothalamic-pituitary-adrenal axis and behavioral dysfunction following early binge-like prenatal alcohol exposure in mice. *Alcohol*. https://doi.org/10.1016/j.alcohol.2015.01.005

Wiggs, L., & France, K. (2000). Behavioural treatments for sleep problems in children and adolescents with physical illness, psychological problems or intellectual disabilities. *Sleep Medicine Reviews*. https://doi.org/10.1053/smrv.1999.0094

Wilckens, K. A., Woo, S. G., Kirk, A. R., Erickson, K. I., & Wheeler, M. E. (2014). Role of sleep continuity and total sleep time in executive function across the adult lifespan. *Psychology and Aging*. https://doi.org/10.1037/a0037234

Wilks, T., Gerber, R. J., & Erdie-Lalena, C. (2010). Developmental milestones: Cognitive development. *Pediatrics in Review*. https://doi.org/10.1542/pir.31-9-364

Willford, J. A., Leech, S. L., & Day, N. L. (2006). Moderate prenatal alcohol exposure and cognitive status of children at age 10. *Alcoholism: Clinical and Experimental Research*, *30*(6), 1051–1059. https://doi.org/10.1111/j.1530-0277.2006.00119.x

Williams, P., Catterick, M., & Calder, E. (2012). "As I see it..." Using social media to bring out the voices of people with FASD, their families and carers. *Journal of Population Therapeutics and Clinical Pharmacology*.

Williams, S. E., & Horst, J. S. (2014). Goodnight book: Sleep consolidation improves word learning via storybooks. *Frontiers in Psychology*. https://doi.org/10.3389/fpsyg.2014.00184

Willoughby, K. A., Sheard, E. D., Nash, K., & Rovet, J. (2008). Effects of prenatal alcohol exposure on hippocampal volume, verbal learning, and verbal and spatial recall in late childhood. *J Int Neuropsychol Soc*, *14*(6), 1022–1033. https://doi.org/S1355617708081368 [pii]\r10.1017/S1355617708081368 [doi]

Wolke, D., & Lereya, S. T. (2014). Bullying and parasomnias: A longitudinal cohort study. *Pediatrics*. https://doi.org/10.1542/peds.2014-1295

World Health Organization. (2014). Global Status Report on Alcohol and Health. Retrieved September 1, 2017, from http://apps.who.int/iris/bitstream/10665/112736/1/9789240692763_eng.pdf

World Health Organization. (2017). Prevention of harm caused by alcohol exposure in pregnancy. Retrieved April 8, 2020, from http://www.euro.who.int/__data/assets/pdf_file/0005/318074/Prevention-harm-caused-alcohol-exposure-pregnancy.pdf

Yafai, A. F., Verrier, D., & Reidy, L. (2014). Social conformity and autism spectrum disorder: A child-friendly take on a classic study. *Autism*. https://doi.org/10.1177/1362361313508023

Yerys, B. E., Hepburn, S. L., Pennington, B. F., & Rogers, S. J. (2007). Executive function in preschoolers with autism: Evidence consistent with a secondary deficit. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-006-0250-7

Yeung, M. K., Lee, T. L., & Chan, A. S. (2019). Right-lateralized frontal activation underlies successful updating of verbal working memory in adolescents with high-functioning autism spectrum disorder. *Biological Psychology*. https://doi.org/10.1016/j.biopsycho.2019.107743

Young, T., Peppard, P. E., & Gottlieb, D. J. (2002). Epidemiology of obstructive sleep apnea: A population health perspective. *American Journal of Respiratory and Critical Care Medicine*. https://doi.org/10.1164/rccm.2109080

Zainal, H., & Magiati, I. (2019). A Comparison Between Caregiver-Reported Anxiety and Other Emotional and Behavioral Difficulties in Children and Adolescents with Autism Spectrum Disorders Attending Specialist or Mainstream Schools. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-016-2792-7

Zhang, Y., Hedo, R., Rivera, A., Rull, R., Richardson, S., & Tu, X. M. (2019). Post hoc power analysis: Is it an informative and meaningful analysis? *General Psychiatry*. https://doi.org/10.1136/gpsych-2019-100069

Zwaigenbaum, L. (2014). The intriguing relationship between cerebral palsy and autism. *Developmental Medicine and Child Neurology*. https://doi.org/10.1111/dmcn.12274

Appendix

Appendix I:

Content and frequency of nightmares by group. This question was asked as part of the battery of questionnaires. Not all children experienced nightmares but of those who did, children with FASD tend to experience more persecutory nightmares than children with Autism.

Diagnosis	Does your child have nightmares? If so, please describe the content and frequency.
TD	Random content. Could be me leaving could be monsters. Could be about going to school. Usually weekly.
TD	Very rarely, last time she dreamed our puppy had died.
TD	At least once a week, they tend to involve wolves, aliens or family members going away/being hurt.
TD	Rarely at the minute and usually he will get up out of bed but not fully awake, needs consoling but will go back to bed easily and fall back to sleep.
TD	May call out for Mummy or Daddy once every couple of weeks. Will sometimes talk in sleep but make no sense.
TD	Occasionally about 1 a month. She can't remember the content.
TD	Yes, he is just been able to tell us that he dreams that monsters are eating people. More often he wakes crying repeatedly (up to 10 times a night) calling for me and tells us that he feels sad.
TD	Nothing I would call a nightmare, but she calls them nightmares. They sound like random dreams, with some running away.
TD	Separation monthly.
TD	Dead people, ghosts, it can happen a couple of times per month.
TD	Every now and then. Normally about something happening to close family or the pets.
TD	The content can vary, and he doesn't always remember. Depending on our routine they are infrequent as he suffers from night terrors, so we monitor things closely.
TD	Very often most nights speak about being chased by a dog.
TD	School worries.
TD	Sporadic. Maybe every 3 -5 weeks. No regular pattern. Sometimes link to tv.
TD	Once a year maybe. Sometimes involving monsters.
TD	He has nightmares very sporadically, but he doesn't want to talk about them.
TD	Occasional due to anxiety, issues at school and stress of preparing for GCSE's.
FASD	Crying screaming thrashing about not often.
FASD	Sometimes, alone, Vikings.
FASD	He sometimes has nightmares. Maybe once a week.
FASD	Yes. Every night. She wakes up screaming and sweating at least once. She seems phased out and will not talk she will however follow instructions. She can't remember what her nightmares are about and will not talk about them the next day.
FASD	Few times a month for a few consecutive nights then none for a while. Content is not clear.
FASD	Occasional nightmares, something that may be worrying him.
FASD	Occasionally.
FASD	Yes. Always monsters chasing him. Usually once or twice a week.
FASD	Yes, related to past experiences, about 2-4 times per week.
FASD	He tells me he has nightmares most nights. He dreams people die or he dies. He dreams he is alone and can't find anyone. He feels he can't come and get me or call out for help as he thinks there are people in the house who will come and kill him.
FASD	Occasionally about monsters and zombies.
FASD	Regularly. Scary witches. Ghosts.
FASD	One every 2 or so weeks. Dreams of being taken by a stranger.
FASD	Once twice a month, she can never remember but she's shouting at somebody in her sleep.
FASD	Being chased, maybe twice a week.
FASD	Sometimes, being chased or chasing, fighting others, knives or clowns. Less frequent in last year and a half.
FASD	She will shout out in her sleep and talks a lot.
FASD	Usually involving boys fighting over her, once a week.
FASD	Has nocturnal epilepsy. Used to have when younger. Now has waking fear palpitation.
FASD	Yes, more than 2 to 3 times a week.
FASD	None that he talks about.
FASD	Yes - vivid dreams about zombies and monsters are common.
FASD	She can't tell me the content. 5 times a week approx.
FASD	Maybe, but she cannot tell us.
FASD	House break in.
FASD	Not sure, will sometimes wake up very upset.
FASD	Being 'robbed' from me.
FASD	Not often. Once a month perhaps. Often dreams foxes have eaten our chickens. Or a fox jumps into his bedroom window. Or fox staring at him through his 2nd floor bedroom window. Sometimes dreams of giants smashing things up in his bedroom. Or dreams of thieves breaking in and stealing his toys and precious cuddly toys. Sometimes monsters or dinosaurs.
FASD	Rarely but if does being chased.
FASD	Yes, but she is unable to explain the content.

FASD	Yes, and wets bed at same time. Content is varied but can be being chased, about once a month it wakes her up.
FASD	Yes, about twice a week he will have bad dream. He is usually shouting 'get off me' and pleading. We go and stroke his head and tell he's at home in bed and is safe.
FASD	Yes 1-week approx. The past.
FASD	Sometimes not as frequent at the moment but talks a lot in his sleep.
FASD	Not as bad recently. Used to wake and be inconsolable, sometimes self-harming.
FASD	Approx. Twice a week. Usually about bad guys or monsters.
FASD	Occasionally no idea what they are about she says bad guys.
FASD	Occasionally....Mum dying.
FASD	Yes, big presence in his room, disturbed by noise.
FASD	Not being able to get something.
FASD	2-3 per month he tells me he has had a nightmare, maybe has them more but doesn't say. They always seem to be about him, his brother and his mum but he can't explain anymore. Suffered neglect while living with mother because of drug and alcohol misuse.
FASD	Sometimes but not clear what the nightmare was about as she doesn't remember, or she can't describe it.
FASD	Sometimes he will say I had a bad dream last night.
FASD	Monsters people in his head telling him to do bad things. At least once a week.
FASD	They have reduced following two and a half years of psychotherapy, but they are nightmares of red buttons, trolls, robots.
FASD	Yes, less frequently now, but approx. Every 3 weeks or so. He is unable to tell us the content.
FASD	Not that he says, he's only mentioned a few in the past but can't remember them
FASD	Yes. Very abstract not very specific.
FASD	Possibly 3-4 times a month Usually someone chasing him or catching him.
FASD	Yes, quite regular, about his siblings, the dog, his toys dying.
FASD	Usually twice a week shouting n muttering in sleep is noted but child will not recall a nightmare. Once a fortnight usually a nightmare about her safety or my safety.
FASD	Yes, he does. Can be very large insects chasing him. Being killed, shot.
FASD	Every night.
FASD	Every night. Mostly about me dying or there being people in the house that will kill him. Lots of his nightmares don't make sense.
FASD	Most night. Dreams about skeletons or the monster that eats babies that lives at school.
FASD	Most nights. Used to be an insomniac before going on risperidone.
FASD	Every night not recalled.
FASD	Monsters 2 times a week.
FASD	Yes at least once a week often every night. People or monsters chasing him.
AUTISM	Not sure if he has nightmares but he shouts out throughout the night and tosses and turns.
AUTISM	1 per week but has gone through phases of having lots. V scared of dark so often needs lights on or gets the fear when wakes at night. When he wakes after midnight, he rarely seems that sleepy and I'm not sure he's going to go back to sleep. He seems v alert.
AUTISM	Rarely, cannot recall content.
AUTISM	Yes often. He doesn't usually want to say but he often dreams of someone in the family or him dying. He goes through phases where he will have nightmares and night terrors every night and other phase where he doesn't have them for a while. He doesn't like closing his eyes or want to go to sleep for fear of nightmares and if he has one in the night, he won't go back to sleep for fear of it happening again.
AUTISM	Yes - almost every night. He doesn't want to describe it when he wakes. Later he may say it's about something from TV or event that's happened. He struggles to switch off the fear and so needs us to sleep with him to get back and stay asleep.
AUTISM	Yes, about once a week, they are always linked to abandonment- being left at a railway station or about waking and no one else being at home.
AUTISM	Yes. And infrequent once a week if that.
AUTISM	Aliens are coming to get him!
AUTISM	She says she has usually if someone has shown her something or she has seen something by accident. Can be 3-4 times a week or none. No pattern. Gets scared by noises.
AUTISM	Approx. Once every 2-3 weeks.
AUTISM	Always. Car crashes. Death. Torture. Being left alone.
AUTISM	Yes, recurring after suffering trauma. Can be up to 4 times a week.
AUTISM	2/3 times a night.
AUTISM	Yes, sometimes, but content almost never disclosed, just 'scary'.
AUTISM	Patches of nightmares, subject not always disclosed. A couple of times a man who followed son and friend in school and in wood and clearing and had fireballs for hands.
AUTISM	I think he sometimes has nightmares, but he is unable to explain the content of his dreams. This occurs probably 2 or 3 times a week.

AUTISM	Sometimes he does; he rarely remembers but they seem to involve him being chased. He went through a rough patch when someone at school told him about 'Five Nights at Freddie's', he was anxious and had nightmares about that for a while.
AUTISM	Nightmares 2-3 times a week usually of some form of harm happening to family member.
AUTISM	Sometimes - only a few times a month. He does talk in his sleep though and sleep walk more frequently.
AUTISM	Over past few months since starting high school has been happening about 10 times a month.
AUTISM	Yes, probably 2 to 3 times a week. Sometimes night terrors but this is lessening with age.
AUTISM	Apparently most nights but he can't describe them.
AUTISM	Occasional nightmare about being lost and unable to find people or being chased by wolves.
AUTISM	Wakes crying saying had bad dream a hand full of times a year.

Appendix II: Recruitment materials

Sloth Scientists

Sloth Scientist workshops are a series of interactive activity workshops for children, running every Saturday between the 28th April and 4th of August at the UCL Institute of Education.

Children are introduced to the fascinating world of the mind and sleep, via Professor Slothington, who sleeps up to 20 hours a day!

Children will be guided through some fun and creative activities designed to make them think about the world around them. They then take part in a series of computer and brain games activities, while we get the opportunity to learn about children's sleep, attention, memory and language.

Children aged between 6-13 welcome to attend. Preference given to children on the Autism or Fetal Alcohol Spectrum.

Email: rabya.mughal.14@ucl.ac.uk
www.lilaslab.com/sloth-scientists

Please Keep This For Your Information

Dear Parents,

Thank you for taking part in this study.

Your participation will help us find the link between how well children sleep, and how well they are able to regulate their emotions, or learn things at school.

This study is being carried out at the UCL Institute of Education, Department of Psychology and Human development.

What Happens Next?

1. Fill in and return the Consent Form and Questionnaire.

Please find enclosed a consent form, and questionnaire with multiple choice questions. These questions are about your child's sleep, behaviour, emotions, attachment and executive function (planning/ memory/ organisation skills). Please fill in this questionnaire as soon as possible, as it is only after you have completed the questionnaire that we are able to continue with the study.

2. Your child will take part in the activities (cognitive testing).

You child will take part in the following activities: 1) British Picture Vocabulary Scale (measuring vocabulary); 2) Raven's Progressive Matrices (Measuring IQ); 3) Continuous Performance Task (measuring attention span); 4) Digit Span Test (measuring working memory). These will be carried out at school at an appropriate time. If you would like to be present whilst these are taking place please indicate this in the consent form. You will be informed of the date and time of your child's test.

3. Your child will come home with an actiwatch (depending on the availability of equipment).

On the day of the activities/ testing, your child may be wearing an actiwatch. This is a small accelerometer, worn on the wrist, that measures how well your child sleeps at night. I will be present at home time in the playground if you have any questions about the watch. It cannot be removed until you cut the plastic, and is waterproof so can be worn in the bath, shower, swimming, etc. For the best results, it should be worn all week, however one **normal** night is the minimum amount. If your child does not have a normal night of sleep, it should be worn for longer. Please ensure that your child does not tamper with the straps. Please note there may be a waiting time for the watch as there is a shortage of equipment.

4. You will receive a report.

After the study is finished, you will receive a detailed report on your child's sleep, behaviour, emotions, memory, executive functioning, IQ, language and attention.

Please ensure that you have completed and returned the questionnaire as soon as possible. If you have any questions, please feel free to drop me an email/ find me at home time.

Kind regards,

Rabya Mughal
rabya.mughal.14@ucl.ac.uk

Lifespan Learning and Sleep Laboratory
UCL Institute of Education

Appendix III: Consent Form

Consent Form

The Lifespan Learning and Sleep Laboratory
Department of Psychology and Human Development
UCL Institute of Education

Please read the following carefully.

Project Title: Sleep, Anxiety, Executive Function and Behaviour in Children.

Information for Parents.

What is the purpose of this research?
Thank you for agreeing to take part in this research. The aim of this research is to find whether there is a link between sleep problems, anxiety, executive function, and behaviour in children. There are two parts to this study. The **first part** is completing the questionnaire attached to this consent form. The **second part** is a study involving some cognitive and sleep measurements of your child.

Do I have to take part?
Taking part in this study is voluntary and you are free to exit it at any time you wish. Allowing your child to take part in the cognitive and sleep measurements is also voluntary. You or your child may withdraw at any point.

What do I have to do?
1. In the following pages you will be asked a series of questions on your child's health, sleeping habits, emotions, and behaviour. You will also be asked background questions. Should you wish to do so, you can provide your name and contact details so that your child's results may be sent to you.
2. Your child will then be given a set of cognitive measurements. These cognitive measurements will take place during school time. You are welcome to attend whilst these take place. The cognitive measurements are: 1) the British Picture Vocabulary Scale (a measurement of language); 2) A Continuous Performance Task (a measurement of attention); 3) Ravens Progressive Matrices (a measurement of IQ); 4) The Digit Span Test (a measurement of working memory); 5) Actigraphy (a measurement of your child's sleep quality. This is an accelerometer worn as a wristwatch.)

What happens to the information in the project?
All personal information on this questionnaire will remain confidential. Should you wish to leave your contact details you are free to do so. All information given in this questionnaire is confidential, and cannot be accessed by anyone other than the researchers named below. University College London is registered with the Information Commissioner's Office who implements the Data Protection Act 1998. All personal data on participants will be processed in accordance with the provisions of the Data Protection Act 1998.

What happens next?
If you are happy to take part, please sign below. Feedback will be given within two weeks of your completion of this questionnaire. All results will be anonymised. Should the results be published, you will be able to view them on the Lifespan Learning and Sleep Laboratory website:
wwww.lilaslab.com

Researcher contact details:
Rabya Mughal: rabya.mughal.14@ucl.ac.uk;
Supervisor: Dr Dagmara Dimitriou, Reader in Psychology, UCL Institute of Education.
Dr. Dagmara Dimitriou: d.dimitriou@ucl.ac.uk

Consent Form

**If you have any questions or concerns, during or after this study,
or wish to contact an independent person to whom any questions may be directed or
further information may be sought from, please contact:**
UCL Ethics Committee
University College London
Gower Street
London
WC1E 6BT Telephone: 0203 108 8216
Email: ethics@ucl.ac.uk

- *I have read the information above and consent to this study:*
- *I understand I am free to withdraw at any point of this study, and that if I wish to do so, no information from this study will be used:*
- *I understand I can contact the researcher Rabya Mughal at any time for any arising enquiries:*
- *I understand that the results will be shared anonymously and and no participant will be identifiable.*

Signed:

_____

Any notes or comments:

_____
_____
_____
_____
_____
_____

Lifespan Learning and Sleep Laboratory
UCL Institute of Education

Appendix IV: Sleep Diary

_____'s Sleep Diary

(Write your name here)

Fill in these blanks with your information.

I am _____ years old and in _____ grade.

This is the week of _____ _____, _____
(Month) (Date) (Year)

1. Complete Before Going to Bed

- **What did you drink today?**

In the space inside each can, write the number of cans/bottles of caffeinated drinks, such as soda and tea, you had each day of the week. Remember, caffeine in drinks can keep you from sleeping well.

- **Check off any of these activities you did in the HOUR before going to bed.**

	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Read a book							
Used the Computer							
Played with Toys/Games							
Exercised/ Played Sports							
Watched TV							
Played Video Games							
Listened to Music							
Had a Snack							
Took a Bath/ Shower							
Talked on the Phone							
Did Homework							

2. Complete When You Wake Up

• How did you sleep?

Answer the first two questions by circling YES or NO. Write your answer to the last question.

	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Did you have trouble falling asleep?	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No
Did you wake up during the night?	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No
Who or what woke you up during the night?							

• How much sleep did you get last night?

Color in the boxes from the time you fell asleep last night until the time you woke up this morning. Count the number of boxes you colored in to figure out how many hours you slept. Write the number of hours you slept below each day.

EXAMPLE	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
7:30 PM	7:30 PM	7:30 PM	7:30 PM	7:30 PM	7:30 PM	7:30 PM	7:30 PM
8:00 PM	8:00 PM	8:00 PM	8:00 PM	8:00 PM	8:00 PM	8:00 PM	8:00 PM
8:30 PM	8:30 PM	8:30 PM	8:30 PM	8:30 PM	8:30 PM	8:30 PM	8:30 PM
9:00 PM	9:00 PM	9:00 PM	9:00 PM	9:00 PM	9:00 PM	9:00 PM	9:00 PM
9:30 PM	9:30 PM	9:30 PM	9:30 PM	9:30 PM	9:30 PM	9:30 PM	9:30 PM
10:00 PM	10:00 PM	10:00 PM	10:00 PM	10:00 PM	10:00 PM	10:00 PM	10:00 PM
10:30 PM	10:30 PM	10:30 PM	10:30 PM	10:30 PM	10:30 PM	10:30 PM	10:30 PM
11:00 PM	11:00 PM	11:00 PM	11:00 PM	11:00 PM	11:00 PM	11:00 PM	11:00 PM
11:30 PM	11:30 PM	11:30 PM	11:30 PM	11:30 PM	11:30 PM	11:30 PM	11:30 PM
12:00 AM	12:00 AM	12:00 AM	12:00 AM	12:00 AM	12:00 AM	12:00 AM	12:00 AM
12:30 AM	12:30 AM	12:30 AM	12:30 AM	12:30 AM	12:30 AM	12:30 AM	12:30 AM
1:00 AM	1:00 AM	1:00 AM	1:00 AM	1:00 AM	1:00 AM	1:00 AM	1:00 AM
1:30 AM	1:30 AM	1:30 AM	1:30 AM	1:30 AM	1:30 AM	1:30 AM	1:30 AM
2:00 AM	2:00 AM	2:00 AM	2:00 AM	2:00 AM	2:00 AM	2:00 AM	2:00 AM
2:30 AM	2:30 AM	2:30 AM	2:30 AM	2:30 AM	2:30 AM	2:30 AM	2:30 AM
3:00 AM	3:00 AM	3:00 AM	3:00 AM	3:00 AM	3:00 AM	3:00 AM	3:00 AM
3:30 AM	3:30 AM	3:30 AM	3:30 AM	3:30 AM	3:30 AM	3:30 AM	3:30 AM
4:00 AM	4:00 AM	4:00 AM	4:00 AM	4:00 AM	4:00 AM	4:00 AM	4:00 AM
4:30 AM	4:30 AM	4:30 AM	4:30 AM	4:30 AM	4:30 AM	4:30 AM	4:30 AM
5:00 AM	5:00 AM	5:00 AM	5:00 AM	5:00 AM	5:00 AM	5:00 AM	5:00 AM
5:30 AM	5:30 AM	5:30 AM	5:30 AM	5:30 AM	5:30 AM	5:30 AM	5:30 AM
6:00 AM	6:00 AM	6:00 AM	6:00 AM	6:00 AM	6:00 AM	6:00 AM	6:00 AM
6:30 AM	6:30 AM	6:30 AM	6:30 AM	6:30 AM	6:30 AM	6:30 AM	6:30 AM
7:00 AM	7:00 AM	7:00 AM	7:00 AM	7:00 AM	7:00 AM	7:00 AM	7:00 AM
7:30 AM	7:30 AM	7:30 AM	7:30 AM	7:30 AM	7:30 AM	7:30 AM	7:30 AM
8:00 AM	8:00 AM	8:00 AM	8:00 AM	8:00 AM	8:00 AM	8:00 AM	8:00 AM
8:30 AM	8:30 AM	8:30 AM	8:30 AM	8:30 AM	8:30 AM	8:30 AM	8:30 AM
9:00 AM	9:00 AM	9:00 AM	9:00 AM	9:00 AM	9:00 AM	9:00 AM	9:00 AM
9:30 AM	9:30 AM	9:30 AM	9:30 AM	9:30 AM	9:30 AM	9:30 AM	9:30 AM
10:00 AM	10:00 AM	10:00 AM	10:00 AM	10:00 AM	10:00 AM	10:00 AM	10:00 AM
I slept 11 hours.	I slept _____ hours.	I slept _____ hours.	I slept _____ hours.	I slept _____ hours.	I slept _____ hours.	I slept _____ hours.	I slept _____ hours.

3. Complete At The End of the Day

- **How did you feel during the day?**

Color in the boxes up to the number that describes how you felt each day.

- **How much energy did you have today?**

		Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Full of energy	5							
	4							
Some energy	3							
	2							
No energy	1							

- **How awake were you today?**

		Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Wide Awake	5							
	4							
Awake but a little sleepy	3							
	2							
Very sleepy	1							

- **How did you do in school today?**

		Monday	Tuesday	Wednesday	Thursday	Friday
Paid attention in all my classes	5					
	4					
Paid attention some of the time	3					
	2					
Couldn't pay attention	1					

Answer these questions by circling YES or NO

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Did you fall asleep when you didn't mean to?	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No
Did you take a nap?	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No

Appendix V: Report for Parents

The Lifespan Learning and Sleep Laboratory
University College London
25 Woburn Square
London
WC1H 0AA

Dear ***

Thank you for taking the time to participate in this study. Please find your child's results set out below.

Name:
Age at testing: * years * months
Date of Birth: dd/mm/yyyy

Below is a description of the tasks your child completed. On the following pages you will find the results of these tasks.

1) Ravens Progressive Matrices (RPM; Raven 2008).
This is a test of general intelligence, traditionally called an IQ test. Raven's Progressive Matrices measure two components of general intelligence: the capacity to think clearly and make sense of complex data (eductive ability); and the capacity to store and reproduce information (reproductive ability). Children are shown a number of pictures with pieces missing, and are instructed to "find the missing piece". Care must be taken when interpreting these kinds of results as children with more practice will do better at IQ tests.

2) British Picture Vocabulary Scale (BPVSl Dunn, 2009).
This is a test of receptive vocabulary which looks at the child's vocabulary age (i.e if the child knows and understands as many words as other children his own age). Children are shown a series of pictures and are instructed to point out their meanings. Words increase in difficulty throughout the task.

3) Sleep - Actigraphy
Actigraphy is a measurement of a child's movement, translated into sleep quality.
Sleep Efficiency: The quality of sleep. Anything above 80% is good.
Sleep Latency: The amount of time to go from wakefulness to sleep. This should be around 20 minutes.
Wake Bout: Number of (short) wakings during the night.
Mobile Time: The amount of time spent mobile during sleep. This should be below 20%.
Please see separate sheet for sleep analyses.

4) Child Sleep Habits Questionnaire (CSHQ; Owens, Spirito & McGuin, 2000)
This is a commonly used questionnaire that assesses pediatric sleep problems. Information from this questionnaire is grouped into 8 categories: Bedtime Resistance (this includes refusal at bedtimes, 'curtain calls' – for example coming down for a glass of water or one more story etc.); Sleep Onset Delay (a delay in the time between lights out and falling asleep); Sleep Duration; Sleep Anxiety (worries about being in the dark, alone, etc.); Night Waking; Parasomnia (sleep walking/ talking/ grinding teeth etc.); Sleep Disordered Breathing, and Daytime Sleepiness. Set out below are scores for each category, and an overall score. If your child's score is higher than a category or overall score, this is an indication that there is a problem with sleep, which should be referred to a sleep professional through your GP or pediatrician.

5) Spence Children's Anxiety Scale (SCAS; Spence, 1997;1998):
This is a commonly used questionnaire that assesses pediatric anxiety problems. Information from this questionnaire is broken down into several different categories: Separation Anxiety, Social Phobia, Obsessive-Compulsive Disorder, Panic, Physical Injury Fears and Generalised Anxiety Disorder. Set out

below are scores for each category, and an overall score. If your child's score is higher than a category or overall score, this is an indication that there are higher levels of anxiety, which should be seen by a clinical professional.

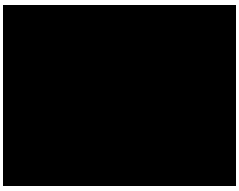
6) The Child Behaviour Checklist (CBCL; Achenbach & Rescorla, 2001)
This is a commonly used questionnaire that assesses children's behaviour. Information from this questionnaire is broken down into several different categories: Withdrawn, Somatic Complaints, Anxious/ Depressed, Social Problems, Thought Problems, Attention Problems, Delinquency and Aggression. Set out below are scores for each category, and an overall score. If your child's score is higher than a category or overall score, this is an indication that there are higher levels of behaviour problems, which should be seen by a clinical professional and addressed/ planned for in daily situations such as at school.

7) The Behaviour Rating Inventory for Executive Function (BRIEF; Goiya & Isquith 2008)
This is a commonly used questionnaire that assesses children's Executive Functioning. Executive functioning is the 'engine' of the brain that allows us to plan, organise, learn and have emotional reactions. Information from this questionnaire is broken down into several different categories: Working Memory (the amount of information that can be held at one time); Shifting (the ability to move from one task to another easily); Planning and Organising; Organisation of Materials; Monitoring (the ability to look outside of the situation); Inhibition (impulsive or erratic behaviour); Initiation ('commonsensical' approaches to daily tasks, and Emotional Control. Clinical scores here are usually used by professionals in conjunction with other psychological measures, and don't usually mean anything on their own.

8) The Attachment Style Classification Questionnaire for Children of Latency Age (Dottan, 2014)
Attachment is the social and biological bond between a baby and a caregiver. It is the basis for many emotional, social and cognitive outcomes later on in life. This questionnaire can give an indication of your child's attachment style, and measures for: Secure, Anxious, Avoidant.

The results contained here are part of my PhD study on sleep, cognition and conduct in children with neurodevelopmental conditions. This PhD is being undertaken at the Department of Psychology and Human Development at the UCL Institute of Education. It is being supervised by Dr Dagmara Dimitriou, Reader in Psychology at UCL. Should you require any further details please use the contact details shown below.

Kind Regards,



Rabya Mughal

PhD Candidate
UCL Institute of Education
rabya.mughal.14@ucl.ac.uk
www.lilaslab.com

	Child's score	Average Score for Age	Interpretation
1) RPM			
RPM Score			*** scored in the * percentile for children aged between * years * months – * years * months.
RPM Age Equivalent			
2) BPVS			
Receptive Vocabulary Score			*** scored in the ** percentile for children aged * years * months – * years * months.
Receptive Vocabulary Age			
3) Sleep			
Sleep Efficiency			
Sleep Latency			
Wake Bouts			
Mobile Time			

(Full actigraphy schedule is attached).

5. The Child Sleep Habits Questionnaire (Owens, Spirito & McGuin, 2000)			
	Child's Score	**Clinical Cut Off**	**Interpretation**
Bedtime resistance		8	
Sleep onset delay		1.5	
Sleep duration		4	
Sleep anxiety		5.5	
Night wakings		3.5	
Parasomnias		8.5	
Sleep disordered breathing		3.5	
Daytime sleepiness		10	
Total		40	

6. The Spence Anxiety Scale (Spence, 1997)			
	Child's Score	**Clinical Cut Off**	**Interpretation**
Panic		7	
Separation Anxiety		3	
Physical Injury Fears		4	
Social Phobia		7	
Obsessive Compulsive		3	
Generalised Anxiety		6	
Total		31-33	

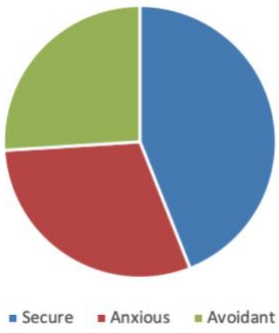
7. The Child Behaviour Checklist (Achenbach & Rescorla, 2001)			
	Child's Score	**Clinical Cut Off**	**Interpretation**
Withdrawn		9	
Somatic Complaints		7	
Anxious/ Depressed		14	
Social Problems		8	
Thought Problems		4	
Attention		11	
Delinquency		7	
Aggression		20	
Total		65-80	

8. The Behaviour Rating Inventory for Executive Function (Gioia, Isquith, Guy & Kenworthy, 2000)			
	Child's Score	**Neurotypical Average**	**Interpretation**
Working Memory		-	
Inhibition		-	
Shifting		-	
Emotional Control		-	
Planning and Organising		-	
Total		65*	

**There is no real 'cut off score' here – this test is used in conjunction with behavioural observations.*

9. The Attachment Style Classification Questionnaire for Children of Latency Age (Dottan, 2014)

Out of the three attachment styles outlined in this questionnaire (Secure, Avoidant, Anxious) *** attachment style has shown as mainly **Secure**, with some Anxious and Avoidant traits**.**



Secure: **/25 (%)**
Anxious: **/25 (%)**
Avoidant: **/25 (%)**