UNIVERSITY OF SOUTHAMPTON

FACULTY OF MEDICINE, HEALTH & LIFE SCIENCES

School of Psychology

Sleep and Neuropsychological Functioning in School Aged Children

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ABSTRACT

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SLEEP AND NEUROPSYCHOLOGICAL FUNCTIONING IN SCHOOL-AGED CHILDREN

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This thesis investigated the relationship between sleep disturbance and neuropsychological functioning in healthy, typically developing children and children with cystic fibrosis (CF). Three research questions were examined in this thesis. The first examined whether sleep disturbance is associated with specific deficits in executive functions or an overall deficit in executive functioning. The second research question examined the relationship between sleep disturbance and behaviour problems. A final research question examined whether sleep disturbance, in the absence of hypoxia, affects executive functioning in a comparable way to sleep disturbance associated with hypoxia.

The first study demonstrated that global executive function (GEF) was significantly lower in healthy children with higher sleep disturbance. Sleep disturbance was not associated with individual performance on executive function tasks.

The second study also examined sleep and executive function in healthy children using a revised battery of neuropsychological tests. Compared to children with low sleep disturbance, children with high sleep disturbance had significantly lower GEF and lower processing speed. Both sleep quantity and sleep quality predicted GEF however sleep quantity explained an additional unique proportion of the variance.

The third study examined sleep in children with cystic fibrosis. When dichotomized into high and low sleep disturbed groups, neither GEF nor processing speed was significantly different between the two groups. The sleep and neuropsychological functioning of children with CF was compared to the healthy, typically developing children from Study 3. There were no significant differences between children with CF and healthy controls on any sleep measures or executive function performance. Nine children with CF underwent one night of polysomnography. A further aim of Study 3 was to examine whether neuropsychological deficits were greater if in the presence of both high sleep disturbance and nocturnal hypoxia. Executive function deficits were worse in children with nocturnal hypoxia, irrespective of whether they had high or low sleep disturbance. In contrast, processing speed deficits were more evident in children with high sleep disturbance, irrespective of whether they had nocturnal hypoxia.

A consistent finding throughout this thesis was that children with higher conduct problems have increased sleep disturbance (measured using parent report and actigraphy).

These findings have implications for children's development; future research examining the effects of sleep disturbance on executive function should consider whether these effects are irreversible.

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List of Acronyms

AASM	American Academy of Sleep Medicine
ADHD	Attention Deficit-Hyperactivity Disorder
AHI	Apnoea-Hypopnoea Index
AWMA	Automated Working Memory Assessment
BRIEF	Behavior Rating Inventory of Executive Function
CANTAB	Cambridge Automated Neuropsychological Test Battery
CBCL	Child Behavior Checklist
CBFV	Cerebral Blood Flow Volume
CF	Cystic Fibrosis
CPAP	Continuous Positive Airways Pressure
CPRS	Connors Parent Rating Scale
CSHQ	Child's Sleep Habits Questionnaire
DAS	Differential Abilities Scale
DS	Daytime Sleepiness
DV	Dependent Variable
EEG	Electroencephalogram
ECG	Electrocardiogram
EMG	Electromyogram
EF	Executive Function
FEV	Forced Expiratory Volume
GEF	Global Executive Function
GLM	General Linear Model
ICSD-R	International Classification of Sleep Disorders-Revised
IED	Intra/Extra Dimensional
IQR	Interquartile Range
IV	Independent Variable
LWE	Long Wake Episodes
MANOVA	Multivariate Analysis of Variance
MDN	Median
NEPSY	Neuropsychological
NREM	Non-Rapid Eye Movement
NHS	National Health Service
NW	Night Wakings
OSA	Obstructive Sleep Apnoea

PFC	Prefrontal Cortex
PRM	Pattern Recognition Memory
PSG	Polysomnography
PSQ	Paediatric Sleep Questionnaire
REM	Rapid Eye Movement
RVP	Rapid Visual Processing
RDI	Respiratory Disturbance Index
SA	Sleep Anxiety
SD	Sleep Duration
SDB	Sleep Disordered Breathing
SDQ	Strengths & Difficulties Questionnaire
SOD	Sleep-Onset Delay
SOC	Stockings of Cambridge
SSP	Spatial Span
SWM	Spatial Working Memory
TEA-Ch	Test of Everyday Attention for Children
TST	Total Sleep Time
WCST	Wisconsin Card Sorting Task
WISC	Weschler Intelligence Scales for Children

Declaration of Authorship

I, **Simone Lisa Holley**

declare that the thesis entitled

Sleep and Neuropsychological Functioning in School-Aged Children

and the work presented in the thesis are both my own, and have been generated by me as the result of my own original research. I confirm that:

- this work was done wholly or mainly while in candidature for a research degree at this University;
- where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;
- where I have consulted the published work of others, this is always clearly attributed;
- where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;
- I have acknowledged all main sources of help;
- where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;
- none of this work has been published before submission

Signed: ……..

Date:…….

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CHAPTER 1 INTRODUCTION

1.1. General Introduction

Humans spend almost one third of their lives sleeping, a behaviour that is thought to occur in almost all animals and certainly in all mammals. The urge to sleep is regular, compelling, and often uncontrollable, leading some researches to argue that sleep must be crucial to human functioning. Exactly what those functions are, however, has yet to be decisively answered. The obvious solution would be to sleep deprive someone for as long as possible, however this would have serious ethical implications, especially given the evidence that approximately two weeks sleep deprivation is fatal in a rat (Everson, Bergmann, & Rechtschaffen, 1989). There are several documented cases of adults who have attempted to deprive themselves of sleep for as long as possible, but these have often been attention-seeking incidences that have not been experimentally controlled. The longest recorded incidence of sleep deprivation is 268 hours (Horne, 1988). Numerous empirical studies have explored the consequences of sleep deprivation in humans, yet, despite years of research, some authors argue that the precise purpose of sleep has not been identified (Horne, 1988; Stickgold, 2000). There are many theories that attempt to identify the purpose that sleep serves, although it is likely that there are multiple separate systems that are influenced by the sleep process: endocrine, immunologic, and thermoregulatory.

This thesis explores the theory that one function of sleep is to provide rest and recovery to the prefrontal cortex, and that inadequate recovery will affect neuropsychological functions believed to be subserved by the prefrontal cortex (Horne, 1988). From a developmental perspective, this theory could have serious implications for the neuropsychological development and cognitive functioning of children.

1.2. Thesis Aims

The rationale behind this thesis is the theory regarding a possible relationship between sleep, the frontal lobes, executive functioning, and behaviour. Several theorists (Beebe & Gozal, 2002; Horne, 1988) have argued that during sleep, the frontal cortex is deactivated, a process that enables recovery and restoration. The hypothesis suggests that if the frontal cortex does not get the respite it requires (due to disrupted sleep) this can have adverse effects on functions and behaviours that are subserved by the frontal

lobes such as attention, memory, planning. There are several published studies examining this hypothesis in adult populations, however, only a few studies have been examined whether children may be particularly vulnerable to such a relationship.

Many previous studies of neuropsychological functioning and sleep in children only examine one or two areas of cognition and/or behaviour. This thesis aims to investigate a broad range of abilities that are described as executive functions, as well as behavioural manifestations of executive dysfunction. The primary aim of this thesis is to examine whether sleep disturbance is associated with specific deficits in executive function (EF) or whether executive functioning *overall* is affected by sleep disturbance. A further question that this thesis investigates is whether sleep disturbance, in the absence of sleep disordered breathing problems, affected neuropsychological functioning, in a comparable way to sleep disturbance associated with sleep-disordered breathing. To address these questions, both typically developing children and children at risk of sleep disturbance and respiratory problems (specifically children with cystic fibrosis) were studied.

1.3. Outline of Thesis

This thesis is organised into nine chapters. Chapter 2 begins with an overview of what constitutes normal sleep, and the methodologies used to measure sleep. This is followed by a discussion of abnormal sleep and sleep problems, and the factors that may contribute to sleep disturbance and sleep difficulties. The effects of sleep loss, particularly the cognitive and behavioural consequences of sleep disturbance, are examined, both those associated with sleep disordered breathing and general sleep disturbance. The chapter ends with a discussion of the mechanisms that may contribute to the relationship between sleep disturbance and reduced neurocognitive performance. Chapter 3 focuses upon EF: descriptions of what is meant by the term 'executive functions', how executive functions are organised, how EF develop in childhood, and methodological issues in measuring EF. The literature regarding the concept of executive functioning and its development throughout childhood is also examined. Chapter 3 introduces the reader to common childhood conditions that are risk factors for sleep disturbance with a particular emphasis on sleep in children with cystic fibrosis. Chapter 5 reports the findings from Study 1: sleep and neuropsychological functioning in healthy, typically developing children. Chapter 6 reports the findings from Study 2 – also investigating sleep and neuropsychological functioning in a general population sample of children but using a different battery of neuropsychological tests. Chapter 7 reports the findings from Study 3 – sleep and neuropsychological functioning in children with cystic fibrosis, and Chapter 8 reports the findings from a subsample of these children who underwent one night of full polysomnography. Chapter 9 provides a discussion and summary of the thesis, as well as suggestions for future directions.

CHAPTER 2 SLEEP

2.1. THE SLEEP CYCLE

On a daily basis, almost every member of the animal kingdom will experience a behaviour that involves the transition from a highly conscious state to a markedly reduced level of awareness where one is disengaged and almost unresponsive to the environment. Sleep is a behaviour that is often uncontrollable, and along with eating and drinking, it is a fundamental biological behaviour. However, unlike the purpose of eating and drinking – to provide essential nutrients and energy - the precise function of sleep remains unanswered. Historically, it was believed that sleep represented a dormant, inactive state of the brain, however with the advent of technologies to record electrical brain activity using the electroencephalogram (EEG), came the knowledge that electrical activity during sleep is distinct from that when awake. Kleitman and Aserinsky were the first to demonstrate that sleep consisted of EEG activity not observed during waking (1953, 1955). They also showed that two distinct types of EEG activity were associated with two different forms of sleep: slow-wave sleep (also commonly referred to as NREM sleep) and rapid-eye movement sleep (or REM sleep). The work of Kletiman & Aserinsky was advanced by Rechtschaffen & Kales (Rechtschaffen & Kales, 1968) who developed a system for scoring the sleep stages based on the EEG pattern; this criterion is still in use today.

2.1.1. The Sleep EEG

Figure 1 illustrates the change in EEG activity from wakefulness to sleep. During wakefulness, EEG activity consists of two types of firing patterns: alpha and beta waves. Alpha waves (8-12 Hz) are high-amplitude and synchronised, occurring during periods of relaxation and rest. Beta waves, which are more common, are low-amplitude, irregular, and slightly faster at 13-30 Hz. In contrast, sleep is characterised by a cycle of slow-wave activity (under 3.5 Hz) followed by a period of REM sleep during which electrical activity changes so that the EEG is very much like that of light non-REM sleep. Slow-wave sleep is subdivided into three stages that become increasingly deeper. Prior to 2007, sleep technologists would distinguish between stage 3 and stage 4 sleep but new guidelines published by The American Academy of Sleep Medicine now recommend scoring stage 3 and 4 together.

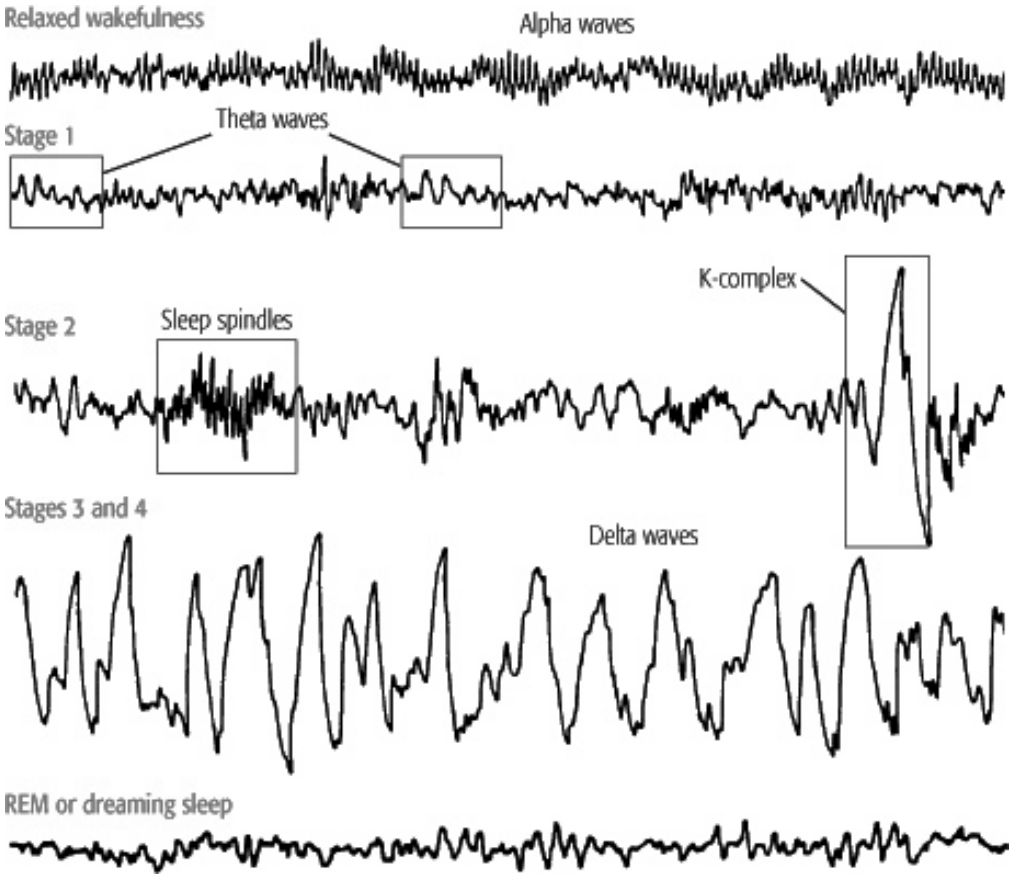

Figure 1 EEG activity during sleep and wake

2.1.2. Sleep Architecture

The onset of sleep begins with stage 1, at first fast alpha waves characterise the EEG representing a typical drowsy state, these are gradually replaced by lower frequency theta waves (4-7 Hz). Stage 1 is typically very brief rapidly progressing to stage 2 where sleep onset is formally defined. Stage 2 is also characterised by theta waves but with the addition of sleep spindles that are brief bursts of 12-15 Hz activity. As sleep becomes deeper, slow but high-amplitude delta waves (1-4 Hz) become evident and by stage 3, delta waves dominate the EEG pattern, with this sleep being the deepest and most difficult to wake somebody from.

Following this cycle of slow-wave sleep, which typically lasts around 80 minutes, there is a sudden transformation in the EEG pattern with brain waves becoming desynchronised, faster and of lower amplitude. This represents the transition to REM sleep where electrical activity in the brain is representative of the beta pattern observed during aroused, awake states. The first REM sleep stage lasts for 3-5 minutes but they become progressively longer throughout the night. REM sleep was so named due to the

observation that during this type of sleep, movements under the eyelid occur that are similar to those when awake. In addition, cerebral blood flow and oxygen consumption increase almost to the levels of waking. There is a loss of muscle tone, with odd twitches of eyes, faces, fingers and toes but the rest of body appears paralysed. There is also an increase in activation of the sympathetic nervous system (cardiac, blood pressure and breathing). Dreaming is highly prevalent in REM sleep: 80% of subjects will report dreaming if woken during REM sleep, with dreams often vivid, disjointed, and illogical. Some people will also report dreaming if woken from slow-wave sleep but such dreams are less vivid, and tend to be static and repetitive. This cycle of NREM and REM sleep repeats itself throughout the night, with each cycle lasting about 90-110 minutes.

2.1.2.1. Development of sleep architecture

There are distinct differences in the architecture of infant and adult sleep. Sleep cycles in infants are quite different; a newborn will sleep for about 16 hours per day with each sleep cycle lasting around 50-60 minutes (as opposed to the 90 minute adult sleep cycle). In addition, infants often enter REM-like sleep at the start of their sleep period in contrast to adults whose first REM cycle comes after a period of NREM sleep (Stores, 2001). Furthermore, a newborn will spend around 50% of his/her sleep time in REM-like sleep, a proportion that is even higher in premature infants (Curzi-Dascalova, Peirano, & Morel-Kahn, 1988). The ratio of REM to non-REM sleep steadily decreases throughout infancy so that by the age of one, REM sleep makes up around 30% of total sleep, and continues to decrease throughout the second year of life until it reaches the adult proportion of 20-25% (Coble, Kupfer, Taska, & Kane, 1984). Qualitative differences also arise later in life around the age of 50. As noted above, by the age of 50, the amount of sleep time is reduced to around 4-6 hours; the majority of the sleep time lost predominately consists of stage 3 and 4 slow-wave sleep (Gaudreau, Carrier, & Montplaisir, 2001). The decline in stage 3 and 4 slow wave sleep continues with age so that by the age of 90, it has virtually disappeared (Bliwise, 1993).

2.1.3. Development Of Sleep Patterns

Unfortunately for parents, infants are not born with the ability to sleep for a single consolidated period during the night. Instead, sleep is distributed throughout the day and night, interspersed with varying periods of wakefulness. Night waking is an accepted phenomenon during infancy, particularly in the early months when an infants' stomach

is very small and unable to store large amounts of milk to sustain the child through the night. Almost from birth, the number of sleeping hours steadily decreases, so that by the age of one, an infant will be sleeping on average 14 hours per day and by the age of five a child will typically sleep for 10 - 11 hours a day. The shift from a multiphasic sleep pattern to that of an almost single period of sleep during the night is also a gradual process, dependent upon physiological and biological mechanisms such as the circadian rhythm and homeostasis, as well as psychosocial mechanisms such as parenting. At puberty, there are significant alterations to the sleep process, thought to be due to hormonal changes that regulate the sleep pattern (Carskadon, Acebo, & Jenni, 2004). During adolescence, the number of hours spent sleeping decreases to around 6- 8 hours of sleep each night; hence this could be seen as the point when the sleep process matures, as it remains stable for the next 20 years or more. Although the sleep process remains stable for many adult years, it is by no means the end of the development of the sleep cycle. By the age of 50, there is a distinct reduction in the number of hours slept from 6-8 hours in early adulthood to 4-6 hours a night (Horne, 1988).

2.2. Sleep Methodology

As noted above, EEG enables researchers to record electrical activity of the brain during sleep. In recent years, several new methods have been developed that use different physiological outcomes for the data. The following section will outline the various methods available to measure sleep.

2.2.1. Polysomnography

Polysomnography (PSG) is a particularly detailed assessment carried out overnight that provides information regarding several physiological changes that occur during sleep as well as changes to the brain waves. Due to its comprehensive appraisal, PSG is often earmarked as the 'gold standard' in the assessment of sleep, particularly for diagnosing sleep-disordered breathing problems. A typical PSG will document the following: electrical activity in the brain with electroencephalogram (EEG); electrical activity of the heart with electrocardiogram (ECG); chest movements; movements of the eye with electrooculagram (EMG); muscle activity and limb movements with electromyogram (EMG); airflow and respiratory measurements; blood oxygen saturation (pulse oximetry).

Although PSG is thought to be the most reliable and accurate method to evaluate sleep architecture, disorders of sleep, and respiratory parameters, it is intrusive and very costly, estimated at $1000 - $1400 (Chervin, Murman, Malow, & Totten, 1999) and also requires specialist trained technicians and a sleep laboratory. In addition, some authors argue that the intrusive nature of the assessment method risks disruption to the natural sleep pattern and is not representative of sleep in the home (Portier et al., 2000). PSG is routinely only performed for one or two nights, hence it is unlikely to provide representative information about social aspects of sleep that may affect a persons sleep habits. Although limited by the restricted view that only one or two nights of assessment can provide, for the investigation of certain sleep disorders, such as periodic limb movement disorder, PSG is the only reliable and valid method of assessment.

There are several alternatives to a full laboratory PSG that have been developed to monitor sleep in the home environment. The high cost and time-consuming nature of laboratory PSG will mean that in some cases it may not be the most appropriate method to measure sleep. Jacob and Brouillette (2000) argue that full PSG may not be necessary for diagnosing obstructive sleep apnoea (discussed below) in healthy children. Portable units have been developed that can measure EEG and EMG as well as cardiorespiratory events. These are often used alongside audio and video recordings that can provide information on arousals.

2.2.2. Actigraphy

Activity-based measurement using an actigraph is considered by some authors as a reliable method for characterising sleep-wake patterns in both disordered and normal sleep. An actigraph is a small watch-like device, typically worn on the wrist (or ankle) that uses a miniaturised acceleration sensor to translate physical motion to a numerical representation. Most devices contain a piezo-electric beam that detects movement in two or three axes. The device has an internal memory that stores data in epochs (usually 1 minute intervals) and data can be collected for extended periods of time (usually 1 week or longer). Sadeh and Acebo (2002) recommend that actigraphy be carried out for at least five nights to reliably characterise an individual's sleep-wake pattern. The data from the actigraph is then fed into a computer algorithm that automatically generates sleep-wake scores and statistics. Validation studies have demonstrated a 90% agreement rate between actigraphy and PSG for normal subjects (Sadeh, Alster, Urbach, & Lavie, 1989).

2.2.2.1. Benefits of actigraphy

When compared to PSG, actigraphy is a relatively cheap and simple technology to use. As such, it can be used in large-scale studies and/or where multiple nights of data are required. Furthermore, the non-invasive nature of the device makes it ideal for use with infants and children, as well as populations who may find invasive procedures such as PSG difficult to endure. Due to its benefits, actigraphy is recognised by the American Academy of Sleep Medicine (AASM) as a reliable and valid method for detecting normal sleep in healthy populations and may be a useful adjunct in detecting certain sleep disorders such as restless legs syndrome (Littner et al., 2003).

2.2.2.2. Limitations of actigraphy

Although the AASM regard actigraphy as a useful method for normal sleep, they propose it is less reliable at detecting disturbed sleep, and is not recommended for the routine diagnosis or assessment of sleep disorders. Compared to PSG, actigraphy provides limited data regarding sleep characteristics and is unable to provide any information regarding breathing-related problems during sleep. Actigraphy has a tendency to overestimate sleep time, as the device is unable to distinguish between periods of sleep and periods of extreme nocturnal inactivity. This has led some authors to suggest that actigraphy is not an accurate sleep-wake indicator (Pollak, Tryon, Nagaraja, & Dzwonczyk, 2001).

A further problem in actigraphy research is the lack of established measures and psychometric data. Multiple actigraph devices are available that differ with regards to mechanical properties, sensitivity, and sampling. Studies comparing two different devices have reported significant differences the sensitivity of the devices to record movements (Pollak, Stokes, & Wagner, 1998). Another problem concerns the lack of a standardised data method to analyse the data generated from actigraphy. Computer algorithms have been developed that are used to automatically score the actigraphy records generating sleep-wake measures. A number of different algorithms are available that have typically been designed for use with specific actigraph brands. Some actigraphy outcome measures have been validated against PSG buy many have not had any such validation (Sadeh & Acebo, 2002) and not all devices have been validated against PSG.

2.2.2.3. Actigraphy compared to polysomnography

As already noted, there is a substantial cost difference between actigraphy and PSG. Although actigraphy has limited application, it is nonetheless a useful methodology for identifying sleep-wake in a large sample. Sadeh, Raviv, & Gruber (2000) used actigraphy to establish normative data on the sleep-wake patterns of school-age children. They examined 140 children for 5 nights and found an average of two night-wakings each night, indicating a consistent phenomenon from infancy to early adolescence. Almost every fifth child was defined as experiencing significant sleep problems based on their objective definitions, criteria that they propose as norms to be used in subsequent research. Most of the children with a problem were not identified as such by the parents or children and such a study would have been costly and time consuming if they had used PSG.

Kushida et al. (2001) reviewed the validity of using actigraphy compared to PSG and found that as the quality and quantity of sleep declines, so does the accuracy of the actigraphy data. Actigraphy overestimated total sleep time by 1-1.8 hours and sleep efficiency by 12.1-29.1%. However, when actigraphy and subjective report was combined, the data were not significantly different from polysomnography data in detecting total sleep time and sleep efficiency. Using a high-threshold algorithm (more activity is required to score wake) the actigraph was as good as PSG in detecting awakenings. However, Pollak et al. (2001) argue that actigraphy is not an accurate indicator of sleep and wake. They report data showing that the predictive value of actigraphy to identify sleep and wake was only 62% when compared with PSG. However, this was data collected throughout the day and night. When they analysed the data from night-time only, the predictive value of the actigraphy increased to 86%.

2.2.3. Self-report

Although actigraphy is considerably more cost-effective than PSG, it still requires specific equipment and is time consuming: Sadeh, Gruber, & Raviv (2002) recommend that the actigraph be worn for five consecutive nights in order to obtain a realistic evaluation of the sleep pattern. If a quick and simple estimate of sleep is required then questionnaires are a quick and economical alternative method for sleep research. Questionnaires can also provide longitudinal and social information about sleep patterns over several months.

In the developmental literature, two questionnaires in particular have reliability and validity data available: the Pediatric Sleep Questionnaire (Chervin, Hedger, Dillon, & Pituch, 2000) and the Children's Sleep Habits Questionnaire (Owens, Spirito, & McGuinn, 2000b).The PSQ contains 70 closed-question items regarding sleep behaviours in general that are responded to with either yes, no, or don't know. A 22-item sleep-disordered breathing (SDB) subscale is derived from the PSQ that has been validated for use in diagnosing sleep-related breathing disorders where PSG is unavailable or impractical.

2.2.3.1. The Children's Sleep Habits Questionnaire

The CSHQ is a similar parent-report sleep screening instrument that has demonstrated satisfactory internal consistency, test re-test reliability, and validity (Owens et al., 2000b). The CSHQ contains 45-items examining the sleep behaviours of school-aged children over a typical week. The frequency of a variety of sleep behaviours is responded to on a 3-point Likert type scale (rarely = 0-1 nights per week; sometimes = 2-4 nights per week; usually 5-7 nights per week). The CSHQ yields a total sleep score, with higher scores reflecting greater total sleep disturbance. Eight subscales are also derived from the questionnaire that relate to Bedtime Resistance, Sleep Duration, Sleep Onset Delay, Sleep Anxiety, Night Wakings, Sleep-Disordered Breathing, Parasomnias, and Daytime Sleepiness. Unlike PSG and actigraphy, questionnaire methods are not objective nor are they based on any physiological recordings. For younger children, such reports are completed by the parent (although the CSHQ is also available in a self-report form for 7yrs and above). Parental reports of the child's sleep may be constrained by how often the parent monitors or observes the child's sleep and biases may occur due to limitations of the parent's knowledge regarding sleep problems.

2.2.3.2. Parental report versus actigraphy

Previous studies have demonstrated inconsistencies when parental report is compared to actigraphy. An assessment of actigraphy and parental ratings of sleep in children with attention-deficit/hyperactivity disorder (ADHD) found that according to parental reports, children with ADHD had significantly more sleep problems (such as longer sleep-onset and restless sleep) compared to control children (Corkum, Tannock, Moldofsky, Hogg-Johnson, & Humphries, 2001). However, these findings were not verified by the actigraphy data, which did not show any significant differences in the sleep parameters of ADHD and normal children. The authors suggest that the lack of

correspondence between parental and actigraphy sleep reports, particularly with regards to sleep-onset and night wakings, may reflect the challenging behaviour typical of children with ADHD. Disruptive behaviour characterises children with ADHD, hence difficult behaviour around bedtime and during the night, may be interpreted by parents as a sleep problem, rather than as behaviour typical of a child with ADHD.

Similar results were reported by Wiggs, Montgomery, & Stores (2005) when assessing the sleep patterns of unmedicated children with subtypes of ADHD compared to controls, using actigraphy and parental-report. Sleep disturbance was frequently reported by parents of children with ADHD subtypes, particularly the initiation of sleep. Furthermore, a detailed clinical sleep history, obtained from parents, suggested that 88% of the ADHD group had an unidentified and untreated sleep disorder. Despite these findings, there were no significant differences in actigraphy data between ADHD and controls. However, the author's have not reported subjective sleep data for the control group, therefore it is possible that parents of the control children would have also have reported a wide range of sleep problems. Correlational analyses between subjective and objective data showed that parents of children with ADHD were good at estimating wake-up times, but not at estimating sleep-onset or night wakings. The author's concluded that "parents of children with ADHD may not be accurate reporters of their child's sleep pattern and/or the sleep disturbances that come to parents' attention are not best detected by actigraphy" (Wiggs et al., 2005, p. 1437).

Many studies reporting the accuracy of subjective reports compared to actigraphy have been conducted with abnormal populations, such as those described above. Few studies have examined the reliability of questionnaires to identify sleep habits in healthy, normal children. Correlations between actigraphy and parental reports in a study of normal children (mean age 5.5 years) indicated that parents were able to accurately identify sleep onset and offset but were less accurate in their estimation of sleep quality measures such as night wakings (Tikotzky & Sadeh, 2001). Werner et al (2008) compared sleep-wake patterns in children aged 4-7 years, as measured using actigraphy, parental diary and parental questionnaire. They found satisfactory agreement between actigraphy and diary for sleep start time, sleep end time, and assumed sleep, but the agreement between actigraphy and parental report of nocturnal wake times was inadequate. The agreement rates between the questionnaire and actigraphy were poor,

and the authors conclude that questionnaires are insufficient for collecting information on children's sleep.

To summarise, there are three main methods used in children's sleep research, PSG provides the most accurate physiological data but is expensive, time-consuming, invasive, and typically only provides information on one or two nights of sleep (that may not be particularly representative). In contrast, actigraphy is a cheaper alternative that yields objective physiological data on a child's natural sleep-wake pattern with minimal disruption. Questionnaires, although subjective, also have a place in sleep research particularly for acquiring longitudinal and social information regarding sleep habits and problems or for screening participants before using PSG or where large-scale data collection is required. Kushida et al. (2001) suggest that subjective reports used in conjunction with actigraphy can be useful in diagnosing sleep disorders.

2.3. Sleep Disturbance

A major issue in the study of sleep concerns how sleep disturbance is defined. In the published literature the term sleep disturbance is applied to studies that examine both disrupted sleep (i.e. sleep interrupted by arousals), as well as sleep loss due to a restriction on the amount of time spent sleeping – both acute sleep deprivation (experimental studies often look at the effects of very short sleep times such as 5 hours) and chronic sleep derivation – weeks and months of having less sleep than is recommended. A contributing factor is the lack of a universal definition of normal sleep: the notion of what constitutes normal sleep is very subjective and varies with development. The Royal College of Psychiatrists advises that children need around 9 - 10 hours of sleep per night, whereas adults need 7-8 hours per night. In contrast, Horne (1988) suggests that adults sleep for longer than necessary. He proposes that it is only the first 4-6 hours of sleep that is essential, any further time sleeping is superfluous from a physiological restoration viewpoint. Horne (1988) suggests that the common sleep period of 6-8 hours has arisen from cultural and social factors. The concept of normal sleep also varies between cultures. As noted by Owens (2004), many countries have bi-phasic sleep patterns that incorporate a period of sleep during the daytime, and a shorter period of sleep in the night-time. From a clinical perspective the International Classification of Sleep Disorders (ICSD) manual (American Sleep Disorders Association. Diagnostic Classification Steering Committee, 1990) provides information

on how to define clinical sleep disturbance. However, there will inevitably be cases of sleep disturbance that either do not meet the necessary criteria required to make a particular diagnosis, or are outside the scope of ICSD. In addition, there are complex and different ways in which the sleep cycle can be disturbed. Sleep loss can be either total (i.e. no sleep at all) or partial (only a few hours sleep due to inadequate bedtimes). In addition, frequent arousals during the sleep period may cause sleep loss, despite sufficient time in bed. Inappropriate timing of the sleep period may also lead to sleep disruption, a problem that typically occurs in adults who work shifts. It is yet to be determined whether different types of sleep loss have different behavioural and/or cognitive consequences. Neither has it been established which aspect of sleep is most important from a restorative viewpoint (Stores, 2001).

2.3.1. Clinical Sleep Disturbance

The International Classification of Sleep Disorders (ICSD-R) catalogues around 80 sleep disorders classified into three major categories: dyssomnias, parasomnias, and other sleep disorders associated with mental, neurological or other medical disorders. ICSD-R is not a child-specific catalogue and includes many disorders that are only applicable to adult patients.

2.3.1.1. Dyssomnias

Dyssomnias are primary sleep disorders that produce either difficulty initiating or maintaining sleep or excessive sleepiness; hence, they often result in insufficient or excessive sleep. Dyssomnias are further subdivided into intrinsic dyssomnias, extrinsic dyssomnias, and circadian rhythm disorders which are described in the next sections followed by an overview of parasomnias and other sleep disorders.

2.3.1.2. Intrinsic dyssomnias

As the name suggests, intrinsic dyssomnias originate or develop within the body or arise from causes within the body. Examples include certain types of insomnias, narcolepsy (excessive sleepiness with persistent daytime napping), hypersomnia (a prolonged period of sleep such as 18 hours) and periodic limb movement disorder (PLMD), characterised by periodic episodes of repetitive and highly stereotype limb movements during sleep. A common childhood intrinsic dyssomnia is restless legs syndrome (RLS), a disorder characterised by disagreeable leg sensations occurring prior to sleep onset that cause an almost irresistible urge to move the legs. Obstructive sleep apnoea (OSA)

is another intrinsic dyssomnia. OSA is characterised by repetitive episodes of upper airway obstruction that occur during sleep, usually associated with a reduction in blood oxygen saturation. Loud snoring, brief gasps and periods of silence are typical symptoms. Typical complaints include feeling un-refreshed in the morning despite having an adequate period of sleep, and excessive daytime sleepiness. OSA is common in overweight adults, whereas in children it is typically associated with enlarged adenoids and tonsils, with the signs and symptoms of OSA often more subtle than in an adult. Current research suggests there may be a relationship between OSA and neurocognitive deficits, hence there is a growing body of research in the psychological literature examining whether children with sleep-disordered breathing difficulties have reduced cognition (Blunden, Lushington, & Kennedy, 2001). This relationship and the possible mechanisms by which this association may occur is discussed in subsequent sections.

2.3.1.3. Extrinsic dyssomnias

Extrinsic dyssomnias include those disorders that originate or develop from causes outside of the body. Removing the external factors that are producing the sleep disorder will lead to resolution of the sleep problem. Inadequate sleep hygiene is a sleep disorder caused by daily living activities that are inconsistent with the maintenance of good quality sleep and full daytime alertness. Behaviours that may increase arousal include alcohol consumption or caffeine ingestion. Others may be inconsistent with the principles of sleep organization, such as ensuring appropriate bedroom temperature and lighting, or suitable furniture.

Of particular relevance to the study of childhood sleep problems is limit-setting sleep disorder. As suggested by its name, this disorder is characterised by the inadequate enforcement of bedtimes (usually by the parent) which then leads the child to delay or refuse going to bed at an appropriate time. It is estimated to affect 5-10% of the childhood population (Ferber & Guilleminault, 1987).

Sleep-onset association disorder is another typically child-orientated extrinsic dyssomnia although it can occur in adults as well. The main feature of the disorder is that sleep is only initiated under certain conditions, e.g. when the parent is in the room. Other extrinsic dyssomnias known to affect children include food allergy insomnia and nocturnal eating (and/or drinking) syndrome.

2.3.1.4. Circadian rhythm sleep disorders

The third subgroup of dyssomnias are termed circadian rhythm sleep disorders and share a common underlying chronophysiologic basis. In most instances, the disorder leads to an inability to sleep when needed, expected, or desired. This category includes sleep problems caused by shifts in time zones, perhaps due to air travel (jet-lag) and sleep problems caused by shift-work (shift work sleep disorder). Irregular sleep-wake pattern is a disorder characterised by the absence of any recognisable circadian rhythm, consisting of temporally disorganised and variable episodes of sleeping and waking behaviour. Delayed sleep phase syndrome (DSPS) is also characterised by inappropriate sleep-wake schedules and severe difficulty in getting to sleep and awakening. Unlike irregular sleep-wake pattern, the pattern in DSPS is regular, albeit somewhat delayed in comparison to the desired bedtime.

2.3.1.5. Parasomnias

The second major category of sleep disorders are the parasomnias, not abnormalities of sleep and wake states but are disorders characterised by undesirable phenomena that occur during the sleep cycle and often result in partial arousals or other disturbances that intrude upon the sleep period. Parasomnias are further subdivided into four groups: arousal disorders (such as sleepwalking and sleep terrors), sleep-wake transition disorders (sleep talking), parasomnias usually associated with REM sleep (e.g. nightmares), and other parasomnias. From a developmental perspective, those of particular importance are sleep enuresis (bed-wetting), primary snoring (due to its potential association with neurocognitive deficits, discussed in section 2.7, infant sleep apnoea, and sudden infant death syndrome.

2.3.1.6. Other sleep disorders

The third major category in the ICSD-R consists of sleep disorders associated with mental, neurological, or other medical disorders. They are not primary sleep disorders but refer to sleep related manifestations of psychiatric or medical conditions. For example, anxiety and mood disorders are typically associated with significant sleep disruption. Several neurological disorders are also associated with sleep disturbance particularly cerebral degenerative disorders (e.g. Huntingdon's disease), Parkinsonism, and dementia. Other medical conditions such as asthma can result in frequent night-time arousals due to nocturnal symptoms such as chronic cough.

Although, the ICSD-R lists many medical conditions that are associated with sleep disturbance, several other childhood conditions not listed in the manual have also been identified. Stores (2001) highlights that sleep problems are particularly common in children with learning disabilities, although this is not mentioned in ICSD-R. Children with ADHD have also been identified as at-risk from sleep problems (Chervin et al., 2002). Similarly, children with pervasive developmental disorders (PDD) such as autism are also more prone to sleep problems compared to their healthy counterparts (Honomichl, Goodlin-Jones, Burnham, Gaylor, & Anders, 2002) as are children with epilepsy (Stores, Wiggs, & Campling, 1998). Hence, there is a need for this classification system to be revised and updated in line with contemporary research and findings.

2.3.2. Sleep Disturbance in Children

Significant sleep disturbance may go undetected in childhood whilst the behavioural and cognitive consequences may be clearly observable. It is estimated that around 20-30% of children experience significant sleep problems from infancy to adolescence (Zuckerman, Stevenson, & Bailey, 1987). As noted above, there are numerous causes of sleep disturbance in children: biological, physiological, psychological, and social. Some causes are specific to childhood whilst others can be a cause of sleep disturbance at any age. Identifying sleep disturbance in children is important, as it can be a symptom of certain medical conditions (such as obstructive sleep apnoea) or of underlying psychopathology such as ADHD. In addition, there are individual differences in the perception of what constitutes sleep disturbance as well as differences in the classification of sleep disorders at different ages. Stores (2001) points out that there are considerable differences between different ethnic and socioeconomic groups regarding child-rearing practices to develop children's sleep patterns. As noted above, the sleep pattern of a newborn is expected to be multiphasic with little differentiation between day and night. Such a sleep pattern in an adult or even an older child would be considered abnormal behaviour.

2.3.3. Social & Parental Factors In Childhood Sleep Disturbance

The ICSD-R has been criticised as being a predominantly adult-orientated diagnostic tool: there can be considerable differences in the causes and types of sleep disturbance found in children compared to adults (Stores, 2001). In particular, the role of parental

factors highlights a significant difference in the aetiology of adult and child sleep problems. Adults and children may experience identical sleep problems, but the cause of that problem may be completely different. Children are dependent on their parents to develop good sleep hygiene practices - appropriate night-time routines in preparation for sleep, ensuring the sleeping environment is one that is conducive to a good night's sleep, and encouraging positive attitudes towards sleeping. Although the establishment of a single, continuous period of sleep during twilight hours is governed by biological and physiological mechanisms, the importance of social and parental factors is also critical.

Several childhood sleep problems are caused by parenting factors. In early childhood, the parent must teach the child to go to bed at an appropriate time, in an appropriate manner, to sleep alone, and without constant attention, especially if woken. Often this requires the use of behavioural techniques in limit-setting. If the parent is unable (or unwilling) to ensure these practices are learnt at an early age, they may face sleep problems later in childhood.

Children, especially at a very early age, are also dependent upon the parent (or other caregiver) to recognise if there is a problem, and then seek professional help. Recognising sleep difficulties will be influenced by the caregiver's knowledge and education regarding normal sleep behaviour as well as the ability to do so. For instance, many parents of children who are diagnosed with OSA were unaware that their child was having apnoeic episodes during sleep as the parent was never in the child's room when they were heard (Stores, 2001).

Sleep problems in children have also been associated with other psychosocial factors such as maternal depressive mood. In a longitudinal study, Zuckerman et al. (1987) examined a variety of psychosocial and demographical variables in infants aged 8-months. They found that maternal depression was the only measured variable that was significantly associated with persistent sleep problems at age three. Subsequent work has confirmed this association: Hiscock & Wake (2001) also found the only significant characteristic associated with maternal depression was maternal report of a child sleep problem. It has not yet been established whether childhood sleep problems are caused by maternal depression: the mothers' lack of sleep due to continued night-time disturbance may result in increased depressed feelings. Alternatively, Zuckerman et al.

(1987) suggest there may be differences in the parenting methods of depressed mothers compared to non-depressed mothers that lead to increased prevalence of child sleep problems. Exposure to parental marital conflict has also been associated with reduced sleep duration and poorer sleep quality (El-Sheikh, Buckhalt, Mize, & Acebo, 2006).

2.4. Cultural Influences on Childhood Sleep

American and western European views of childrearing may overly dominate health professional's attitudes towards problematic sleep behaviour (McKenna, Loughlin, Carroll, & Marcus, 2000). For instance, co-sleeping is often thought to be undesirable in America and the UK. In contrast several cultures around the globe (such as Japan and Guatemala) consider co-sleeping to be the norm. Jenni & O'Connor (2005) also argue that many childhood sleep problems are "based on culturally constructed definitions and expectations" rather than being rooted in sleep biology (Jenni & O'Connor, 2005, p.205). For instance they cite a study by Morelli of the highland Mayan community in Guatemala, where there are no bedtime routines and children fall asleep when they are sleepy. Mayan mothers expressed shock at being told of the American trend of putting infants and young children to sleep alone. In Japan, co-sleeping is considered the norm (in contrast to the US).

2.5. The Neuropsychological Consequences of Sleep disturbance in Adults

2.5.1. Introduction

This section begins with a very brief overview of research findings in adult populations followed by a detailed examination of the cognitive and behavioural effects of sleep loss in children. There is a phenomenal amount of literature examining the effects of sleep loss in adults, going back as far as 1896 (Patrick & Gilbert, 1896, cited by Durmer & Dinges, 2005). Comparing studies can be difficult due to variations in the type of sleep loss being studied: research is generally divided into studies examining long-term total sleep deprivation, short-term total sleep deprivation, and partial sleep deprivation. Furthermore, the measures of neurocognitive performance following sleep deprivation also vary widely among studies, making comparisons across studies problematic.

2.5.2. What is Sleep Loss?

As already noted above, a major issue in sleep research is the lack of a clear definition regarding what constitutes sleep loss or sleep deprivation. Some researchers argue that chronic sleep loss is common in the general population (Bonnet & Arand, 2003). The definition of sleep loss depends, of course, on one's definition of what constitutes a normal amount of sleep. Horne (1988) suggests that the commonly quoted guideline figure of 6-8 hours as a requirement for adults is misleading and he believes there is no evidence that we need such an amount of sleep. Horne (1988) argues that humans only need 4 or 5 hours of sleep, which he refers to as 'core' sleep. Any sleep obtained after this period he refers to as 'optional' sleep and is based on a behavioural need rather than a physiological one. Hence studies examining the consequences of having only 5 hours sleep per night may not be examining the effects of sleep loss at all if Horne's (1988) proposals are accurate. The debate over daily sleep need in humans is also fuelled by a lack of adequate studies examining the cognitive and behavioural effects of chronic daily sleep restriction (Van Dongen, Maislin, Mullington, & Dinges, 2003).

2.5.3. The Effects of Sleep Loss on Adult Cognition

Many early studies examining the effects of sleep loss on cognitive performance attempted to eliminate the 'practice effect' by ensuring that participants were well-rehearsed in the task prior to experimental testing. This procedure was used to ensure that any differences in task performance following sleep deprivation could not be attributed to practice effects. In addition, early sleep researchers suggested that boring, long, tedious, and uninteresting tasks were required to demonstrate sleep loss effects on cognition. Short, interesting, and novel tasks were assumed to be unaffected by sleep loss (Harrison & Horne, 1998; Nilsson et al., 2005). However, it has been argued that in earlier studies, the sensitivity of tests to sleep loss occurred due to tedium and a lack of novelty (Harrison & Horne, 1998). Nonetheless, a meta-analysis of 19 studies examining the effects of sleep deprivation on performance found that sleep deprivation had the greatest negative effects on mood compared to either cognitive or motor performance. Cognitive performance was more affected compared to motor performance. Furthermore, partial sleep deprivation had a much stronger overall effect on functioning compared to short-term or long-term sleep deprivation (Pilcher & Huffcutt, 1996).

More recent research contradicts the assumption that short, novel tasks are unaffected by sleep loss. In particular, a growing body of experimental studies suggest that sleep loss may particularly affect neuropsychological tests orientated towards the prefrontal cortex (PFC). Harrison and Horne (1998) sleep deprived (SD) adults for 36 hours. Compared to non sleep-deprived controls, subsequent performance on two language tasks assumed to have a PFC focus was significantly impaired. SD adults were slower to respond and made more errors in the Haylings test, which requires participants to provide incongruous endings to sentences. SD adults also generated fewer words in a task requiring participants to generate as many verbs as possible to a given noun.

Van Dongen et al. (2003) compared the effects of chronic sleep restriction and total sleep deprivation on various neurobehavioural and physiological functions. Participants were assigned to either total sleep deprivation for 3 days, or chronic sleep restriction for 8, 6, or 4 hours sleep per night for 14 days. Psychomotor vigilance and working memory performance in participants who were sleep deprived (4 or 6 hours) for 14 days, was equivalent to the deficits observed after 2 days of total sleep deprivation. They conclude that humans are not able to adapt to chronic sleep restriction, and that sustained moderate sleep restriction can seriously impair neurobehavioral functioning.

Nilsson et al. (2005) found that sleep deprived participants performed significantly worse on a test of executive functioning – the 'Six Elements' task (SET). The task measures supervisory control of executive functioning and everyday functioning, and was designed as an ecologically valid test to identify impaired functioning among patients with frontal lobe damage. In contrast to previous studies, sleep deprived participants were not impaired on psychomotor vigilance, verbal or visuospatial working memory.

2.5.4. Imaging Studies of Sleep Loss and Neurocognition

Research has also examined *in vivo* brain activity changes and cognitive function during experimentally induced sleep deprivation. Thomas et al. (2000) examined changes in cerebral glucose metabolic rate (CMRglu), a marker for neuronal activity using positron emission topography (PET). During the PET scan, participants performed a serial addition/subtraction task, which required sustained attention, working memory, and arithmetic processing. Following 24 hours of sleep deprivation, significant decreases in

absolute regional CMRglu were found for many brain regions. Of particular interest, is the finding that the prefrontal cortex showed large regional decreases in CMRglu, suggesting a significant deactivation in this area following sleep deprivation. In addition, alertness and cognitive performance was significantly reduced when compared to baseline.

In contrast, a series of studies conducted by Drummond and colleagues showed a somewhat different pattern of results. The studies examined the effects of sleep deprivation on cerebral activation (measured using FMRI) during a verbal learning task (Drummond et al., 2000), an arithmetic task (Drummond et al., 1999), and a divided attention task (Drummond, Gillin, & Brown, 2001). After 35 hours of total sleep deprivation, the verbal learning and divided attention tasks both showed increased PFC cerebral activation as well as activation of other brain regions not recruited during the tasks following a normal night of sleep. In contrast, the arithmetic task showed decreased cerebral activation after 35 hours of sleep deprivation, with no new areas of activation reported. Furthermore, no new areas of brain activation were reported following sleep deprivation when compared to normal sleep. Drummond & Brown (2001) suggest that total sleep deprivation triggers an 'adaptive cerebral compensatory response', whereby the brain recruits additional regions to assist in cognitive processing. In the verbal learning task and the divided attention task, increased activation in the parietal lobes is proposed to be a compensatory mechanism for the loss of activation in the temporal lobes following total sleep deprivation.

These are just a few of the many studies examining the neuropsychological effects of sleep loss in adults. Several papers give a comprehensive account of the effects of sleep deprivation (Bonnet & Arand, 2003; Durmer & Dinges, 2005; Pilcher & Huffcutt, 1996). A detailed examination of the relationship between sleep loss and neuropsychological functioning in children is given in the following sections.

2.6. Neuropsychological Consequences of Sleep disturbance in Children

Research examining the consequences of sleep disturbance in children is generally limited to publications over the last two decades, and, like the research on adult populations, the effects of sleep loss on children's neuropsychological functioning has yet to be comprehensively examined. The following section will firstly examine studies

examining cognitive and behavioural outcomes associated with sleep disturbance in general population samples, typically screened using questionnaire methods. Studies that have used children who show symptoms of sleep-disordered breathing, verified using objective methods such as polysomnography or oximetry, are discussed separately to distinguish between cognitive deficits that may be caused by hypoxia in contrast to general sleep disturbance per se.

2.6.1. Neurocognitive Outcomes Associated with General Sleep Disturbance in Children

In one of the only experimentally controlled studies of sleep restriction in children (Randazzo, Muehlbach, Schweitzer, & Walsh, 1998) 16 children aged 10-14 years were randomly assigned to either 11 hours or 5 hours in bed (in a sleep laboratory) for a single night. Cognitive functions were evaluated the following day, with the sleep-restricted children showing significant impairment on the Wisconsin Card Sorting Task (WCST) and verbal creativity. No differences on memory and learning tasks were found and the authors argue that motivation may have helped to overcome this. Furthermore, these findings should be interpreted with caution due to the small sample size (n=16).

Sadeh, Gruber, & Raviv (2003) examined the effects of 3 nights of sleep restriction and extension on a battery of neuropsychological tests. After sleeping for 2 nights as per normal, children were then randomly assigned to either extend their bedtime by one hour or restrict it by one hour. After 3 consecutive nights of altered sleep schedule children were tested using the Neurobehavioural Evaluation System (NES). Six tasks were included that measure (amongst other things); motor speed, vigilance, sustained attention, response inhibition, working memory. Children who extended their sleep (actual time extended was on average 41 minutes from baseline) performed better (compared to baseline) on tasks of simple digit span, digit forward memory test, and a continuous performance test. Children who restricted their sleep or who had no change in their sleep did not improve from baseline to postintervention testing.

A large-scale study evaluated self-reports of 449 Dutch school children aged between 9 and 14 years (Meijer, Habekothe, & van den Wittenboer, 2000). Sleep quality was assessed using four questions that measured: number of night wakings, sleep latency, sleep latency after awakenings, and perception of sleep quality. Concentration was measured using a paper-and-pencil task and school functioning was assessed using the

School Perception Questionnaire. They did not find any relationship between performance on the concentration task and either time in bed or quality of sleep arguing this could be due to the task being short and simple. However, they did find a significant relationship between school functioning and sleep quality (as measured using the four questions noted above). Furthermore, school functioning was not related to time in bed.

Deficits in working memory have also been associated with poorer sleep quality as measured using actigraphy rather than subjective self-report. Steenari et al. (2003) evaluated the association between sleep and performance on auditory and visual working memory tasks in 60 Finnish children aged 6-13-years of age. They used an n-back task, which allows memory load to be varied. Significant associations were found between task performance and sleep duration, sleep efficiency, and sleep latency, particularly on the highest load levels. Auditory tasks were impaired more than visual tasks. The authors argue this is evidence that poorer sleep quality is related to working memory deficits, however, the n-back task also incorporates a substantial attention component, as they did not measure attention it is difficult to rule out the possibility that the deficits were related to the attention component of the task rather than the working memory component. Furthermore, the study measured sleep using actigraphy for only 4 nights, whereas the minimum recommended period is 5 days (Sadeh & Acebo, 2002).

2.6.2. Behavioural Outcomes Associated with General Sleep Disturbance in Children

In addition to the cognitive outcomes that have been associated with disturbed sleep, research suggests that adverse behavioural profiles may also be associated with disturbed sleep, in particular ADHD. As noted by Cohen-Zion & Ancoli-Israel (2004), the notion that ADHD is associated with sleep disturbance is not new, and goes back as far as 1971. Parents of children diagnosed with ADHD are more likely to report symptoms of sleep disturbance compared to parents of control children, and children with ADHD report more disturbance in their sleep compared to children without ADHD (Owens, Maxim, Nobile, McGuinn, & Msall, 2000a).

Smedje, Broman, & Hetta (2001) also report high rates of behaviour problems in children with sleep problems in a large scale study of children aged 6-8 years of age. Behaviour was assessed using the Strengths & Difficulties Questionnaire (Goodman,

1997) and a parental questionnaire was devised to assess sleep problems. Children with high hyperactivity scores were reported to have more tossing and turning during their sleep. Higher Conduct Problems were associated with more Bedtime Resistance, and increased Emotional Symptoms were associated with difficulties in falling asleep. Overall, 35% of children with global reports of sleep problems were more likely to have significant behaviour problems. These findings are supported by Sadeh et al. (2002) who found that children categorised as 'poor' sleepers (poor sleep efficiency and >3 night wakings) were rated by their parents as having more problems with 'thought disorder' and delinquency (using the Child Behaviour Checklist). Increased teacher ratings of behaviour problems (attention and academic problems) have also been found after one week of experimental sleep restriction – an average sleep period 6 hours compared to baseline of 9 hours (Fallone, Acebo, Seifer, & Carskadon, 2005).

2.6.3. Critique of Existing Research on Neuropsychological Outcomes Associated with General Sleep Disturbance in Children

As already noted, the literature examining the cognitive and behavioural consequences of sleep disturbance (in the absence of sleep-disordered breathing) in children is limited. Two major limitations of the existing research are 1) that most of the studies conducted are correlational, and 2) there is inconsistency in the measures that are used. Of the studies reviewed above, only three have used experimental sleep restriction. To unequivocally demonstrate a cause and effect relationship between sleep disturbance and neuropsychological deficits requires an extended period of experimental sleep restriction, however this design would have serious ethical consequences in young children. Nonetheless, the use of parental questionnaires and self-report measures are valid in that they can provide information about sleep habits over extended time periods, as long as their limitations are acknowledged. A further criticism of studies that have used questionnaires and self-reports concerns the variability of the instruments that have been used to measure sleep. For instance Meijer et al. (2000) used four parental questions to measure sleep disturbance in children. The use of such a small number of questions to identify sleep disturbance will restrict the extent to which any disturbance can be identified. Smedje et al. (2001) devised a parental questionnaire with 15 questions to measure sleep, however the psychometric properties of the questionnaire have not been published. In contrast, Owens et al. (2000) used a 33-item questionnaire that has both reliability and validity data available. The use of differing instruments to measure sleep disturbance in children restricts comparison across studies. Furthermore,

studies should consider using self-report measures of sleep disturbance in children, particularly as parents may not be aware of night wakings.

In addition to the use of differing instruments to measure sleep, studies have also used different methods to assess cognition and behaviour, and the findings both between and within studies have been inconsistence. For example, EF has been measured using the WCST (Randazzo et al., 1998) the NBF (Sadeh et al., 2003), an n-back working memory task (Steenari et al. 2003). In all studies sleep disturbance was associated with selective deficits in performance. It is not clear from the published literature exactly what facets of cognition could be affected by sleep disturbance.

2.6.4. Sleep Disordered Breathing

Sleep-disordered breathing (SDB) is a generic term applied to several disorders that are characterised by varying degrees of upper airway obstruction during sleep. The severity of SDB ranges from primary snoring to obstructive sleep apnoea syndrome (OSA), with diagnosis based on the level of upper airway obstruction. At the mild end of the SDB spectrum is primary snoring, which is characterised by loud upper-airway breathing sounds without any blood gas abnormalities. Primary snoring is commonly associated with enlarged tonsils in children, and does not result in blood gas abnormalities. Upper airway resistance syndrome (UARS) is in the middle range of the SDB spectrum and is also characterised by snoring and a normal blood gas profile, in addition to increased work of breathing and nocturnal arousals. The most severe manifestation of SDB is OSA. A major issue for research examining SDB is the lack of a universally accepted definition for diagnosing OSA. Although the American Academy of Sleep Medicine (AASM) have published guidelines and recommended definitions for SDB problems (Kushida et al., 2005), these guidelines concern adults and their appropriation to children is not known. Furthermore studies do not always utilise these definitions when characterising OSA. A diagnosis of OSA is based upon the number of apnoea-hypopnoea episodes per hour of sleep. AASM recommend that an obstructive apnoea event is defined as cessation of breathing for at least 10 seconds despite obvious respiratory muscle effort. A hypopnoea event is a 10 second event characterised by continued breathing but with a reduction of airflow of at least 30% and with 4% oxygen desaturation. The symptoms of OSA include snoring, cessation of breathing during

sleep, and, excessive daytime sleepiness. OSA also causes hypoxemia, a drop in blood oxygen saturation typically as low as 50%, and an increase in blood carbon dioxide levels (hypercarbia). The severity of OSA is established using the apnoea/hypopnoea index (AHI), which is a measure of the frequency of obstructive events. The AHI is calculated as the number of apnoeas plus the number of hypopnoeas per hour of sleep.

2.6.4.1. OSA in adults

As a consequence of discrepancies in studies, exact estimates on the prevalence of OSA are difficult to obtain as different studies have used different criteria to determine apnoea and hypopnoea events. Recent epidemiological estimates suggest that the prevalence of OSA in the adult population is 4% in men and 2% in women (Stradling & Davies, 2004). Treatment for OSA is usually with nasal Continuous Positive Airway Pressure (CPAP), which delivers a stream of compressed air via a hose to a nasal pillow, nose mask or full-face mask, splinting the airway (keeping it open under air pressure) so that unobstructed breathing becomes possible, reducing and/or preventing apnoeas and hypopnoeas. The major risk factors for OSA in the adult population are being male and overweight.

The health consequences of OSA in adults have been well documented. OSA is associated with increased cardiovascular morbidity and hypertension (El-Ad & Lavie, 2005). A meta-analytical review of studies examining the neuropsychological consequences of OSA in adults found that overall intelligence and verbal functioning is not significantly impaired in adults with untreated OSA. In contrast, adults with untreated OSA show significantly impaired performance on both vigilance tasks and tests of executive functioning (Beebe, Groesz, Wells, Nichols, & McGee, 2003). In addition to specific cognitive impairments, OSA is known to be a significant risk factor for vehicle road accidents, caused by falling asleep at the wheel (George, 2004) and also for accidents in the workplace (Akerstedt, Fredlund, Gillberg, & Jansson, 2002). OSA is also associated with impairments in quality of life including social functioning, and increased rates of depression and anxiety (Engleman & Douglas, 2004). Studies which have attempted to assess treatment-related improvement in neuropsychological functioning have shown some improvements on both mood and neuropsychological performance following CPAP therapy. However, effective treatment does not wholly eliminate any deficit, suggesting that OSA may cause subtle but irreversible brain damage (El-Ad & Lavie, 2005).

2.6.4.2. OSA in children

OSA is thought to affect around 1- 3% of children and habitual snoring around 12% of children (Ali, Pitson, & Stradling, 1993). The major risk factor for OSA in the paediatric population is tonsillar hypertrophy (enlarged tonsils). Neither gender nor obesity, which are the main risk factors for development of the disease in the adult population, are significant risk factors for children (Rosen, 1999). Failure to thrive is known to be an adverse consequence of OSA in children and is thought to be caused by increased energy expenditure, which resolves following adenotonsillectomy (Marcus et al., 1994). An increasing body of research examining the effects of SDB on neurocognitive functioning and behaviour is developing. Research to-date is discussed below followed by an examination of studies that examine whether OSA treatment is effective in reducing the neuropsychological impairments thought to be a consequence of the disease.

2.6.5. Neurocognitive Outcomes Associated with Childhood SDB

Early research suggested a relationship between poor cognition and symptoms of SDB but such studies were typically limited either by small samples, a lack of standardised measures, or lack of objective assessments (Blunden, Lushington, Kennedy, Martin, & Dawson, 2000). Recently, there has been a growth in the number of studies with improved methodology examining the associations between SDB and neuropsychological outcomes, these are examined in detail below.

Preliminary data published by Owens-Stively et al. (1997) found impaired attention in children with OSA. In particular, their results suggest a dose dependent relationship as children classified with moderate/severe OSA (on the basis of PSG) were significantly more affected than children classified as mild OSA. Gozal (1998) found a high prevalence of SDB in children academically ranked in the lowest 10th percentile of their class. Sleep-associated gas exchange abnormalities (as determined from overnight pulse oximetry) were identified in 54 children, 24 of these children underwent adenotonsillectomy. Post-operatively, improvements in academic grades were significantly higher in children who underwent surgery compared to children who were untreated. Consistent with this finding Blunden et al. (2000) found reduced neurocognitive performance in children (aged 5-10 years) who were identified as primary snorers following one night of PSG. Compared to controls, children who snored showed significant deficits in memory, attention, and performance, verbal, and

global IQ scores. The authors highlight the particularly large deficit in selective attention scores and argue that the reduced IQ scores may be the consequence of an attentional deficit. Furthermore, qualitative aspects of sleep as measured using a questionnaire were more closely associated with reduced neurocognitive performance compared to the quantitative aspects of sleep.

Gottlieb et al. (2004) examined SDB symptoms in a community sample of 205 five-year-old children. Parents completed a questionnaire designed to screen for the presence of SDB symptoms and the Pediatric Sleep Questionnaire (PSQ). They found standardised measures of attention, memory, and executive functions (as measured by the NEPSY) were significantly lower in children with symptoms of SDB. A six point loss on IQ was also associated with SDB symptoms, a loss, (as noted by the authors) greater than that observed in children with increased levels of lead in their blood. Of the original sample, 175 also had valid PSG data, with eight of these children showing evidence of OSA. After excluding those children who showed evidence of OSA, SDB symptoms continued to be significantly associated with decreased performance on the NEPSY measures.

Similar findings are reported by O'Brien who also found reduced neurocognition, as measured using the NEPSY, in 5- to 7-year-old children classified as primary snorers. 299 children underwent overnight PSG and a battery of neurobehavioral tests. Children diagnosed with primary snoring were more likely to have problems with attention, anxiety, and depression compared to controls (although these effects were small). Children with primary snoring showed impairments on tests of visuospatial processing, phonological processing, and visual attention, and also on the Differential Ability Scales (DAS) - a general cognitive conceptual ability test. The authors suggest these impairments may be attributed to an increase in sleep fragmentation and decrease in REM sleep percentage in the primary snoring children.

In contrast, Lewin & Dahl (2002) found limited evidence for an association between SDB and poorer cognition. Using the DAS to estimate children's IQ, neither verbal nor non-verbal IQ was significantly impaired in children with OSA compared to healthy controls. However, they did find a significant negative correlation between the DAS verbal scale and the frequency of respiratory disturbance. Consistent with other

researchers they found that children untreated for OSA were significantly impaired on a test of sustained attention compared to healthy controls.

Hill et al. (2006) assessed cerebral blood flow velocity (CBFV), SDB, and neuropsychological function in a sample of snoring children awaiting adenotonsillectomy with healthy controls. Increased CBFV has been associated with neurocognitive deficits in children with sickle cell disease (a condition associated with chronic hypoxemia) and the authors suggest that CBFV may be a marker for vulnerable brain tissue with reduced functioning. Mild SDB was confirmed though one night of PSG in snoring children. CBFV was significantly increased in the snoring children but was not associated with any PSG variables, nor was it associated with any neuropsychological measures. General intellectual function did not differ between the two groups; however, processing speed and visual attention was significantly reduced in the snoring children. These differences were no longer significant when CBFV was used as a covariate. Parental measures of executive function behaviour were all significantly worse in children with SDB, and remained significant even after CBFV was used as a covariate. These findings suggest that factors associated with increased CBFV may explain the association between neurocognitive deficits and SDB.

A large retrospective study suggests that SDB during critical brain development may cause partially irreversible damage, such that the potential for academic achievement is significantly reduced (Gozal & Pope, 2001). Children who were ranked in the bottom quartile of their class were compared to age, gender, and SES matched children ranked in the top quartile of their class. Retrospective parental report of snoring between the ages of 2 and 6 years was significantly more frequent in the low achieving children.

2.6.6. Behavioural Outcomes Associated with Childhood SDB

2.6.6.1. Parental report studies

An association between hyperactivity and sleep problems has been documented by Chervin et al. (2002). Parental reports of sleep problems were obtained using the Pediatric Sleep Questionnaire and child behaviour was evaluated using two measures of ADHD symptomatology. Frequent snoring, more severe daytime sleepiness, and higher scores on the SDB subscale were found in children (particularly young boys) that scored high on measures of inattentiveness and hyperactivity. Data from the same cohort

reported in Chervin et al. (2003) also found that children at high risk of SDB or restless legs syndrome were much more likely to have conduct problems and/or be aggressive, with sleep problems exhibiting a dose-dependent association with severity of conduct problems.

Gottlieb et al. (2004) discussed above, also examined behaviour problems using the Connors Parent Rating Scale-Long form (CPRS), which assesses ADHD symptomatology. Children with parentally-reported symptoms of SDB were rated higher on the ADHD index and cognitive/ inattention scales than children without SDB symptoms. There were no significant differences on ratings of hyperactivity.

2.6.6.2. Oximetry studies

Increased prevalence of behaviour problems in children who habitually snore has also been associated with objective measurements of snoring (Urschitz et al., 2004). In a large study of 1144 children, parent reports were used to screen for snoring symptoms and overnight pulse oximetry recordings were used to determine the presence of intermittent hypoxia. In the short-term, both inattention and hyperactivity were significantly associated with habitual snoring independent of intermittent hypoxia. A 2-year follow-up revealed that children who continued to snore were more likely to display conduct problems, emotional symptoms, peer problems, and hyperactivity-inattention difficulties.

Further support for an association between increased behaviour problems and SDB was found in a cohort that over-represented children from black ethnicity and those who were born pre-term (Rosen et al., 2004). Objective measurement of OSA was taken overnight in the home and snoring was categorised on the basis of information given by the caregiver. Well-validated behavioural measures included the Child Behaviour Checklist (CBCL) and the CPRS. Externalizing and internalizing problem behaviours were significantly more likely in children with OSA and primary snoring. Unlike previous studies, children with SDB were not at higher risk of attentional problems, however, hyperactivity, oppositional, and aggressive behaviour were more problematic. Consistent with Urschitz et al. (2004) increased prevalence of behaviour problems was comparable in children with primary snoring and children with OSA.

Behaviour problems have also been associated with night-time breathing problems in unreferred children aged 6-12 years (Mulvaney et al., 2006). SDB was measured using unattended home polysomnography, and behaviour problems were measured using the CBCL and the CPRS. Children with high RDIs (Respiratory Disturbance Index) also had significantly higher parental reports of problems with attention, social problems, aggression, and oppositional problems.

2.6.6.3. Pre and post adenotonsillectomy studies

A small study of 12 children found significant improvements in behaviour problems (as measured by the Connors scale) and attention following adenotonsillectomy in children identified with SDB (Ali, Pitson, & Stradling, 1996). A larger study of approximately 100 children aged 5-12 years supports this association (Chervin et al., 2006). As noted above, the major risk factor for OSA and SDB in children is enlarged adenoids and tonsils. Previous research examining the extent to which neurobehavioural outcomes improve post-operatively, have been limited in that they have examined only children with severe OSA, despite research suggesting that even mild to moderate SDB is associated with neurobehavioural morbidity. In contrast, this study recruited children who were awaiting adenotonsillectomy, but did not have a history of OSA or treatment for SDB. Children were tested before surgery and post-operatively one year later. Pre-operatively, the children were more hyperactive, and had poorer attention compared to controls (children who underwent surgery other than adenotonsillectomy). After one year, these differences were no longer significant, and those children who underwent adenotonsillectomy showed significant improvement on all measures. However, PSG measures of SDB severity were not associated with any neurobehavioural outcomes, either at baseline or follow-up. The authors suggest this may reflect limitations in standard SDB assessment. Alternatively, it may be that some other variable associated with SDB may underlie the causal relationship between SDB and neurobehavioural deficits.

2.6.7. Critique of Existing Research on Neuropsychological Outcomes Associated with Sleep Disordered Breathing in Children

In contrast to the paucity of studies documenting the adverse effects of sleep disturbance on cognition and behaviour in children, in the absence of any ADB, there are an increasing number studies examining neuropsychological performance in children with OSA and SDB. This is most likely due to the potential medical consequences of the disease, meaning that clinical samples are readily available for research. A wide range of cognitive and behavioural deficits have been associated with SDB in children. Some studies have only used parent report to ascertain the presence of SDB, whereas others have used objective methods such as oximetry or PSG. A review of the effects of intermittent and chronic hypoxia on cognition in childhood concluded that well designed studies have documented the adverse impact of SDB on a range of developmental, behavioural, and academic outcomes even when oxygen desaturation is just below the normal range (Bass et al., 2004). There appears to be little doubt concerning the adverse effects of SDB on behaviour and cognition in childhood, however, the causal mechanisms involved in this association is unclear. Most studies have not shown correlations between PSG variables of SDB and neuropsychological outcomes suggesting the relationship between the SDB and neuropsychological functioning is complex. The major limitations of the research on neuropsychological outcomes associated with general sleep disturbance outlined in 2.6.3 also apply to the SDB research. Studies have used different methods to measure cognition and behaviour making between-study comparisons difficult. Furthermore, there is variability in the methods used to measure SDB symptoms – parental report, pulse oximetry, and PSG. There is also a lack of universally accepted guidelines regarding what constitutes SDB in children, resulting in differing methods to characterise SDB in the studies reviewed.

2.6.8. Summary Of Research Examining Sleep and Neuropsychological Deficits in Children

From the studies reviewed above, there is growing evidence that neuropsychological deficits are associated with sleep disturbance (with and without the presence of underlying medical problems such as SDB). It is noteworthy that studies have found similar patterns of deficits irrespective of the sample – i.e. whether the sample were healthy children or those with SDB. For example deficits in memory and attention have

been associated with SDB (Blunden et al., 2000; Gottlieb et al., 2004) and also with general sleep disturbance (Steenari et al., 2003; Sadeh, Gruber, Raviv, 2003). Higher conduct problems have been found in children with SDB (Chervin et al., 2003) and also in a general population sample (Smedje, Broman, & Hetta, 2001). The similarities in these findings suggests that the pathway or mechanism involved in the association between sleep disturbance and neuropsychological deficits may be similar irrespective of whether SDB is an underlying actor. Given that the pattern of deficits from the different populations is comparable, it is surprising that no studies have attempted to clarify the nature of the relationship between sleep disturbance, SDB, and neuropsychological deficits. However, there have been theoretical suggestions as to the mechanisms that may be involved. The potential mechanisms involved in the relationship between sleep disturbance and neuropsychological deficits is discussed in the next section in terms of the role of the prefrontal cortex and those mechanisms proposed to be involved in SDB: episodic hypoxia, sleep fragmentation caused by repeated arousals, and/or alveolar hypoventilation (Gozal & Pope, 2001).

2.7. The Association between Sleep and Neurocognition

The literature presented above strongly suggests an association between cognition, behaviour, and sleep disturbance, however the precise nature of this relationship is unclear. Researchers have yet to determine the underlying pathophysiological mechanisms by which sleep quality/quantity may affect cognitive functioning and behaviour. Many studies examine the effects of SDB, with an underlying assumption that hypoxia is the source of neuropsychological deficits (Bass et al., 2004). However, the literature presented above suggests general sleep disturbance, with no associated medical condition, is also a risk factor for poorer performance on neuropsychological tasks. These issues raise several important questions about the relative importance of SDB as a pathophysiological mechanism for neuropsychological deficits, which are addressed in this section.

A fundamental question that has not been adequately addressed in the literature concerns whether the neuropsychological and behavioural deficits associated with sleep disturbance and sleep-related breathing problems are caused by different or identical pathways. The literature surrounding SDB has referred to three possible candidates for the neurocognitive deficits associated with OSA: intermittent hypoxia, repeated

arousals, and, hypercarbia[1] (Beebe et al., 2003; Urschitz et al., 2003a). Since general sleep disturbance (in the absence of hypoxia) is associated with neuropsychological deficits, the impact of sleep fragmentation caused by repeated arousals will merit some attention in the following discussion. The following section attempts to address several questions that are raised by these issues: Is there a single pathway responsible for neuropsychological deficits in SDB and general sleep disturbance? Or, are the underlying mechanisms responsible for neuropsychological deficits in SDB different to that in general sleep disturbance? If there are multiple pathways through which sleep can influence neuropsychology, is the pattern of neuropsychological deficits different in SDB to that of general sleep disturbance?

The following section focuses on the literature that attempts to explain neuropsychological deficits in terms of prefrontal dysfunction related to sleep disturbance. This includes evidence from functional neuroimaging data that suggests the prefrontal cortex (PFC) has a specific need for sleep, as well as evidence suggesting that the cognitive and behavioural deficits associated with sleep problems are specific to frontal lobe functioning.

2.7.1. Neuroimaging During Sleep

Functional neuroimaging studies have allowed researchers to explore brain activity during human sleep. In particular, several studies have utilised positron emission topography (PET) methodology. PET is a non-invasive technique that provides visual information regarding functional activity in all brain regions simultaneously. PET can be carried out using different methods, an overview of which is beyond the scope of this thesis, however the optimum method appears to be $H_2{}^{15}O$ (Braun et al., 1997; Maquet, 2000). Regional cerebral blood flow is reduced during NREM sleep compared to wakefulness, although the level of reduction is subject to regional differences. In particular, the frontal areas of the brain show a large reduction in blood flow (Braun et al., 1997) compared to other brain regions. Similarly, REM sleep is characterised by increased activation of certain brain regions but frontal areas remain quiescent. Finelli, Borbely, & Achermann (2001) present EEG data also suggesting there are regional differences in brain activity during sleep. Frontal areas of the brain show a predominance of delta (low-frequency) waves during sleep, suggesting 'frontal deactivation' during sleep.

[1] the presence of an abnormally high level of carbon dioxide in the circulating blood

2.7.2. The Prefrontal Cortex

The neuroimaging data have also been used to support a theory that the PFC is particularly sensitive to the effects of sleep deprivation and that sleep is necessary for adequate recovery of this brain area (Harrison & Horne, 1998; Muzur, Pace-Schott, & Hobson, 2002). Specifically, Muzur et al. (2002) have suggested that deactivation of the PFC occurs due to specific neurotransmitter activity. Deactivation of the PFC is used to explain the phenomenon of disorganised, illogical dream mentation due to executive dysfunction. As a particularly active brain region during wakefulness, deactivation of the PFC also allows it to rest and recover, enabling restoration of executive functioning. Furthermore, sleep deprivation will inhibit the restorative process and hence result in executive dysfunction.

2.7.2.1. Beebe and Gozal's model (2002)

The concept of prefrontal cortical dysfunction as a result of sleep deprivation is comprehensively explored by Beebe & Gozal (2002). They present a theoretical framework linking OSA and neurocognitive deficits in terms of prefrontal cortex dysfunction (see figure 2). The model proposes that sleep disruption and blood gas abnormalities associated with OSA (due to intermittent hypoxia and hypercarbia) triggers cellular and biochemical stresses, which in turn cause cellular injury. These physiological disturbances lead to dysfunction in the prefrontal region of the brain and the behavioural manifestation of this is 'executive dysfunction'. The model accounts for various daytime behaviour difficulties typically observed in sleep-disturbed individuals, such as excessive daytime sleepiness, in terms of disruption to executive functioning. For instance, hyperactivity is frequently reported in children with sleep disturbance (Chervin et al., 2002) and this behaviour is also associated with ADHD, a disorder frequently characterised in terms of executive dysfunction and frontal lobe disorder (Barkley, 1997).

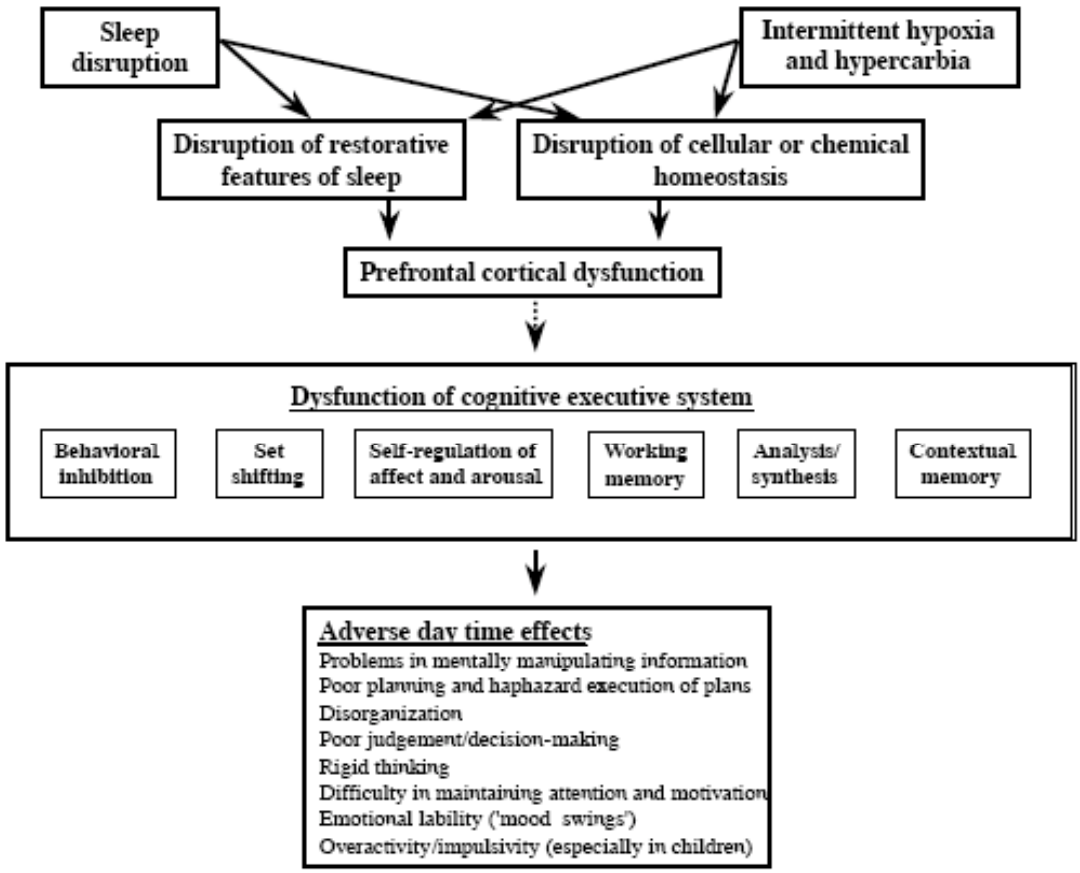

Figure 2 Model of OSA and prefrontal dysfunction (Beebe & Gozal, 2002)

2.7.2.2. Developmental applications of the model

Beebe and Gozal (2002) make reference to both adults and children in their discussion of the proposed model. In particular they highlight the puzzling observation that children with OSA often display daytime hyperactivity in contrast to excessive daytime sleepiness associated with OSA in adults. This observation is accounted for in terms of the association between ADHD and PFC dysfunction. Children with ADHD are more likely to report symptoms of SDB (Chervin, Dillon, Bassetti, Ganoczy, & Pituch, 1997)) and their parents are more likely to report sleep disturbance (Corkum, Tannock, & Moldofsky, 1998). Wiggs, Montgomery, & Stores (2005) were unable to confirm the presence of sleep disturbance (using actigraphy) in a sample of children diagnosed with ADHD. However, they did find that the majority (63 out of 71) of children had an unidentified and untreated sleep disorder such as SDB or sleeplessness. A search of literature has not shown any studies that have combined rigorous diagnosis of ADHD with PSG confirmed sleep disturbance. Beebe and Gozal (2002) also suggest that in children, the vulnerability of the PFC to the effects of OSA may be enhanced due to brain maturation processes. They note that the PFC is one of the last areas of the brain

to mature suggesting that children may be particularly vulnerable to the cognitive and behavioural effects of OSA during early development.

2.7.2.3. Criticisms of the model

As shown in figure 2, the model developed by Beebe & Gozal (2002) proposes that sleep disruption and intermittent hypoxia and hypercarbia are two different causal mechanisms that can both have an influence on the restorative features of sleep and upon cellular and chemical homeostasis. However, the model does not clarify the exact contribution made by the two mechanisms upon each of these outcomes. Does sleep disturbance equally affect the restorative features of sleep and chemical homeostasis? Or does sleep disturbance affect the restoration more than the chemical aspects? Furthermore, the design of the model (with sleep disturbance and hypoxia as two independent factors) would suggest that sleep disturbance alone could invoke prefrontal cortical dysfunction – this implies that hypoxia and hypercarbia are not fundamental elements required to produce executive dysfunction. Recent data suggests that the neurocognitive deficits observed in patients with OSA are no more severe than those in patients with primary snoring. Urschitz et al. (2003a) found an increased risk of poor academic achievement in children who snored compared to non-snorers. Of relevance, was their finding that this relationship persisted after excluding children with desaturation events (drops in blood oxygen levels as determined by nocturnal home pulse oximetry). Moreover, the relationship between academic performance and intermittent hypoxia was not independent of snoring. As noted above, Rosen et al. (2004) also found similar levels of behavioural morbidity in children with OSA and children with only primary snoring. These findings could indicate that snoring alone may cause chronic disruption of sleep architecture, possibly affecting the restoration of the PFC and subsequent executive functioning. Alternatively, it may be that the system of measurement for identifying intermittent hypoxia is not adequate. The clinical thresholds for medical or surgical intervention in SDB is uncertain (Hill et al., 2006) suggesting that the underlying pathophysiology of the condition is poorly understood. It is possible that subtle changes in blood oxygen status are sufficient to induce prefrontal dysfunction – small changes that at present may be disregarded as within the normal range.

Localisation of executive functioning in the PFC is a fundamental assumption of the model. However, the exclusivity of the PFC in executive functioning has been brought

into question. As discussed in Chapter 3, although there is a wealth of evidence suggesting that the prefrontal region of the brain is important in executive functioning, there is nevertheless, evidence that executive functioning extends beyond the prefrontal cortex incorporating other brain regions through multiple neuronal connections (Goldberg, 2001). If the PFC does not solely subserve executive function, the model should be revised to explain how cognitive deficits may arise from sleep disturbance if other regions of the brain are not affected by sleep.

A final criticism of the model concerns the developmental applications of the model. Beebe & Gozal (2002) argue that the model was developed to address developmental issues in OSA. As noted above, they suggest that children may be more vulnerable to the effects of OSA due to under-development of the PFC, however, as discussed in the next section, there is evidence to suggest that it is inappropriate to draw parallels between adult and child frontal lobe function. Furthermore, under-development of brain regions may not necessarily signify increased vulnerability. Developmental neuropsychologists generally agree that there is evidence to suggest that younger brains are able to compensate, reorganise and transfer function from one region to another, when faced with insult or injury (Huttenlocher, 2002; Thomas, 2003). This notion of neural plasticity within the developing brain is discussed below in relation to the suggestion that OSA and SDB may injure the developing brain.

2.8. Maturation of the Frontal Lobes

In contrast to other cortical regions that mature earlier in childhood, development of the frontal regions is more protracted and continues throughout late adolescence and into early adulthood (Romine & Reynolds, 2004). Neuroimaging studies indicate that the prefrontal cortex is most likely the last area of the brain to mature, in particular the dorsolateral prefrontal cortex (Casey, Giedd, & Thomas, 2000). The late development of the frontal lobes is suggested to be a function of evolution: more primitive regions of the brain mature earlier whereas phylogenetically more advanced regions of the brain develop later (Sowell et al., 1999).

Important changes to the structure of the frontal cortex throughout childhood have been well documented: Romine and Reynolds (Romine & Reynolds, 2004) highlight maturation of subcortical prefrontal myelineation and the pruning of synaptic

connections as two particularly noteworthy changes that occur during the early childhood period. Differential changes in regional gray and white matter volume are also of significance. Gray matter represents neuronal cells and is general responsible for information processing, whereas white matter refers to the axons of neurons and is mainly responsible for the transmission of information. A longitudinal study (Giedd et al., 1999) showed increases in gray matter throughout the pre-adolescent period followed by decreases during puberty. In contrast, the maturation of frontal white matter continues throughout childhood and into the second decade (Klingberg, Vaidya, Gabrieli, Moseley, & Hedehus, 1999).

2.8.1.1. Plasticity within the developing brain

> 'If you're going to have brain damage, have it early on.'
> Schneider (1979, in Thomas, 2003)

The above quote describes the Kennard Principle described by Thomas (2003), which proposes that children are less vulnerable to the effects of brain damage compared to adults. In a review of recent literature concerning neural plasticity, Thomas (2003) argues that the brain is capable of significant plasticity which is thought to be greater in childhood. Plasticity changes over time, a change that is poorly understood, nor is plasticity uniform across cognitive domains. Cognitive development is also crucially dependent on environmental interactions, and recovery is not just about neural processes. Of particular relevance to the sleep literature is the finding that frontal brain regions mature later in relation to other structures. Huttenlocher (2002) suggests that synaptogenesis plays a prominent role in developmental plasticity. In infancy there is an explosion of synapse formation, so that the number of synapses is twice that of an adult. This is followed by a period in childhood of pruning, whereby unused connections are eliminated. Huttenlocher (2002) suggests that during this period, the brain is better able to produce adaptive changes to injury or insult, by transferring function to unused, undamaged connections.

2.8.1.2. Plasticity, OSA, and sleep disturbance

Beebe and Gozal (2002) argue that sleep fragmentation and intermittent hypoxia may cause some cellular injury to the developing brain that in turn affects the PFC and

consequently higher-level cognitive functions. However, the notion of neural plasticity would suggest that the developing brain may be able to offer compensatory reorganisation in response to such injury. Furthermore, frontal areas mature later in development, and potentially retain their plasticity for longer (Benes, 2001). In relation to Beebe & Gozal's model, neural plasticity may enable children to better recover from sleep-related PFC dysfunction. This may explain inconsistent results in the literature examining SDB and neuropsychological deficits. The effects of age on plasticity are not clearly understood, hence there may be a critical period whereby children are able to better recover from any adverse effects of SDB and/or sleep disturbance.

2.8.1.3. Sleep, Learning and Memory Consolidation

In addition to the theory that sleep provides respite to certain brain areas, essential for effective functioning of those areas, another related theory concerning the function of sleep is that it contributes to the processing of learning and memories. There is phenomenal interest in the association between sleep and memory consolidation, as demonstrated by an increasing number of publications on the topic. It is beyond the scope of this thesis to give a comprehensive review of the literature, hence this section summarises the key points highlighted in recent reviews on the topic.

As noted by Walker & Stickgold (2006), the suggestion that sleep is important for memory and learning is not recent but one that can be traced back as far as 1801 (Hartley, 1801, in Walker & Stickgold, 2006). Memory consolidation refers to a process that occurs after learning, whereby memories become stabile and resistant to interference and incorporated into long-term memory (Born, Rasch, & Gais, 2006). Researchers often distinguish between declarative memories (factual knowledge) and procedural memories (knowledge concerning how to do something).

Much of the early research examining sleep and memory was underpinned by the assumption that REM sleep was a likely candidate for active processing of memories. Many researchers agree that REM sleep deprivation studies have produced conflicting results (Gais & Born, 2004; Siegel, 2001; Walker & Stickgold, 2006). Many authors agree that the evidence indicates that nondeclarative, procedural memories benefit from REM sleep, whereas declarative memories are enhanced by non-REM sleep (Gais & Born, 2004; Hill, Hogan, & Karmiloff-Smith, 2007; Walker & Stickgold, 2006). Several authors have highlighted the role of the hippocampus (as the brain's memory encoding centre) in sleep and memory consolidation (Drummond et al., 2000; Hill et al.,

2007). A review of the evidence concerning the role of sleep in memory consolidation reports that 83% of published articles on the topic, demonstrate support for the theory that sleep enhances learning and memory consolidation (Stickgold & Walker, 2005). Nonetheless, others disagree that there is conclusive evidence supporting a role for sleep in memory consolidation (Siegel, 2001; Vertes & Siegel, 2005).

It is clear from the literature that the relationship between sleep and memory consolidation is a somewhat controversial and unresolved topic. Furthermore, from a developmental perspective, it is not yet clear whether the research findings are valid to children since most studies have been conducted using animal and adult participants.

2.9. Chapter Summary

This chapter presented an introduction to sleep, including disorders of sleep, and an overview of how sleep may affect neuropsychological functioning. The literature examined suggests that sleep has a fundamental role in brain restoration, specifically that sleep may provide rest for the PFC, a part of the brain that is active and 'online' throughout the day, and hence requires the quiescent night-time period to recover for adequate daytime functioning. This theory is supported by studies showing that sleep disturbance or sleep deprivation is associated with deficits in cognitive abilities and behaviour problems thought to be subserved by the PFC in both adults and children. In particular, research has focused on neuropsychological functions that are assumed to have prefrontal or frontal focus in the brain, often referred to as executive functions. The next chapter shall present a literature review of the concept of 'executive function', with a specific focus on executive function in children.

CHAPTER 3
EXECUTIVE FUNCTION

3.1. INTRODUCTION

Within the domains of both cognitive psychology and neuropsychology there is considerable interest regarding the concept of executive functions (EF) - 'general-purpose, control mechanisms that modulate the operation of various cognitive subprocesses and thereby regulate the dynamics of human cognition' (Miyake et al., 2000). This is just one of many definitions found amongst the plethora of literature examining EF as there is no single, universally accepted characterisation of EF. Miyake et al (2000, pg. 2) propose that 'the field still lacks a compelling theory of executive function'.

The following sections attempt to give an overview of EF research, beginning with definitions of EF and how Baddeley's (1986) concept of working memory has heavily influenced theoretical explanations of EF. This is followed by an overview of concepts frequently postulated as executive functions in the literature and then a discussion of the neuropsychological organisation of EF; including the relationship between EF and the frontal areas of the brain, and the notion of unity and diversity in EF research. This is followed by a brief summary of commonly used measures of EF in adults and a discussion of the extensive methodological issues regarding the measurement of EF. These will be examined briefly with regards to adult research followed by a comprehensive discussion of specific measurement issues when examining executive function in children and additional issues concerning the developmental trajectory of EF throughout childhood.

3.2. WHAT IS EXECUTIVE FUNCTION?

As noted above, there is no universally accepted definition of EF, and a search of the literature generates numerous definitions by many different authors. Miyake et al (2000) refer to EF as mechanisms that control and coordinate other cognitive processes. Likewise, Phillips (1997) refers to executive function as 'a number of interconnecting control processes.' (Phillips, 1997, pg. 193). These 'executive processes' are 'responsible for the control of cognition, and the regulation of behaviour and thought (pg. 192). Anderson (2002) argues that executive function is an 'umbrella term,

encompassing a number of inter-related subskills, necessary for purposeful, goal-directed activity'. Similarly, Hughes & Graham (Hughes & Graham, 2002) propose that rather than referring to a single process, EF is an umbrella term for those complex cognitive processes that are used in 'flexible, goal-directed responses to novel or difficult situations'. Lehto et al. (2003) refer to executive functioning as a 'multidimensional behavioural concept' that encompasses higher-order cognitive processes such as 'goal-directed behaviour, attentional control … and planning'.

A very comprehensive account of EF is given by Rabbitt (1997) who focuses on the distinction between executive and non-executive behaviours. Executive control is required in a situation, not previously encountered, to evaluate and decide upon the best course of action when presented with more than one option. Non-executive behaviour tends to be automatic, although this does not necessarily signify that the behaviour is less complex. Rabbitt (1997) also highlights research indicating that executive behaviour is necessary for efficient and organised recall of material from memory. Furthermore, executive functions are required to initiate new sequences of behaviour, and suppress or inhibit behaviour ensuring that appropriate responses are delivered. Although he gives an account of various 'descriptions' of EF, Rabbit (1997) also emphasises that hypothetical processes such as planning and inhibition do not necessarily represent distinct functional processes, hence, it is not clear whether such processes have any construct validity.

Most authors appear to agree what purpose executive functions should serve; most definitions refer to executive function's being involved in directing and controlling behaviour, particularly in novel situations. However, there appears to be less agreement regarding *which* cognitive processes should be considered 'executive'. There is no universally agreed exhaustive list of EF processes. This creates difficulties for any researcher attempting to investigate executive functioning. Moreover, there is an additional debate concerning whether EF should be conceptualised as one or many processes/behaviours. Hughes & Graham (2002) and Stuss & Alexander (2000) argue that EF should not be considered a single process but a collection of processes. However, Baddeley (1997) suggests that EF, located in the frontal lobes, is responsible for executing cognitive processes such as memory and reasoning. This is suggestive of a single executive function whose purpose is to guide and monitor other processes much the same as the central executive component of the working memory model (Baddeley,

1986). Given that the literature has yet to produce an exhaustive model of EF, it would be inappropriate to examine EF in the context of only one theory. Instead I shall present an overview of those processes widely cited in the literature as referring to executive functions.

Anderson (2002) has proposed a model of EF based on factor analytic studies and clinical neuropsychological knowledge. This model conceptualises executive function as four distinct domains: attentional control, information processing, cognitive flexibility, and goal setting that are conceptualised as an overall control system (see figure 3). The four executive domains are considered as discrete functions that operate collectively when required to execute any particular task. Attentional control exerts a great influence over the other three domains, whereas the cognitive flexibility, goal setting, and information processing are inter-dependent and inter-related. The following section will examine some of these executive processes in detail.

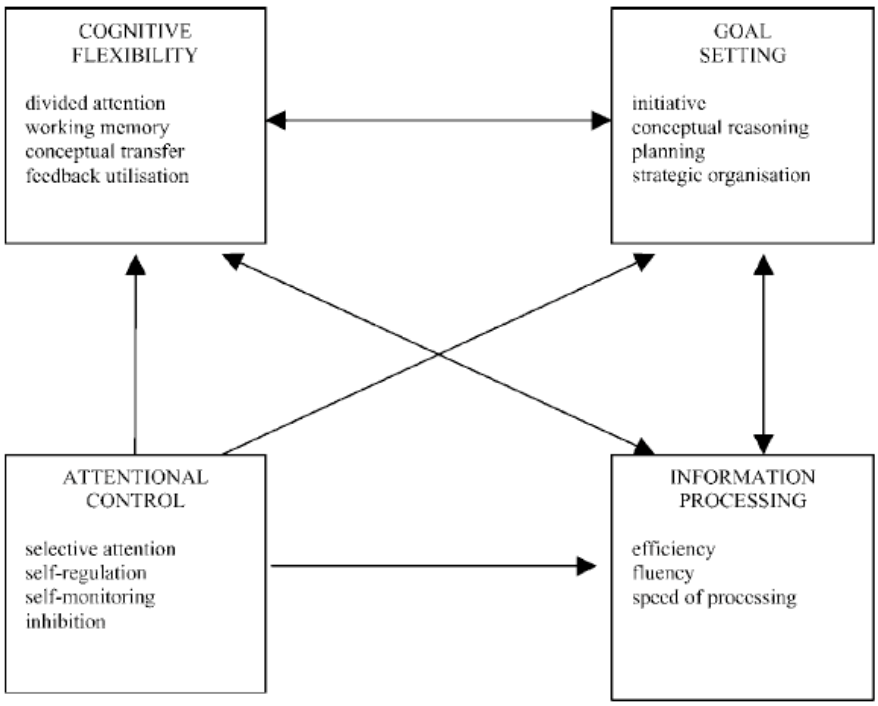

Figure 3 Proposed model of executive function (Anderson, 2002)

3.2.1. Individual Executive Functions

3.2.1.1. Working Memory

The concept of executive function has been heavily influenced by the working memory model initially proposed by Baddeley & Hitch (1974). The first model was posited as an alternative to Atkinson & Shiffrin's (Atkinson & Shiffrin, 1968) earlier concept of working memory as short-term memory store. Atkinson & Shiffrin's (1968) modal model of memory proposed that a sensory buffer feeds information into a limited capacity short-term store (STS), which in turn feeds information into a long-term store. In this model, the STS is a temporary working memory that holds and manipulates information enabling other tasks to be performed. Baddeley & Hitch (1974) proposed that such a model could not account for dual-task experiments where subjects perform a timed reasoning task while concurrently holding sequences of digits in short-term memory. Consequently, Baddeley & Hitch (1974) developed a three-component system model of working memory whereby a limited capacity attentional controller –the central executive – controls incoming information from two slave systems: the phonological loop (originally named the articulatory loop) and the visuospatial sketchpad (originally sketchpad). The phonological loop consists of a temporary storage system that manipulates and retains incoming acoustic and speech-based information and provides an essential rehearsal process, without which information would be lost in a matter of seconds. The visuospatial sketchpad is the slave system that temporarily maintains and manipulates material in terms of its visual or spatial features.

The working memory model was further developed (Baddeley, 1986) by incorporating Norman & Shallice's (1986) model of a supervisory attentional system (SAS) as an interpretation of the central executive – a model that attempts to explain the attentional control of action. The central executive was initially proposed as limited capacity pool of general processing resources that supervises and coordinates the two slave systems. The SAS model assumes that human action is principally controlled by series of schemata and habits that use environmental cues to perform routine tasks – the sudden awareness that one has no recollection of driving the last mile or so along a familiar road is assumed to be a result of such behaviour schematics. The SAS is activated when new or difficult situations are encountered, providing solutions by combining information in long-term memory with existing stimuli (Baddeley, 1996, 2001). Thus, the central executive is proposed to have the capacity to: focus available attentional

capacity; divide attention; and switch attention. More recently, a third subprocess of the central executive has been proposed – the episodic buffer (Baddeley, 2000). This is assumed to represent a limited capacity interface system that uses different codes to interface between the slave systems and long-term memory.

3.2.1.2. Attention

"Everyone knows what attention is. It is the taking possession of the mind in clear and vivid form of what seem several simultaneous objects of trains of thought."

James, 1890, p.403, in (Posner, 2004).

Unfortunately, from a neuropsychological research viewpoint, 'everyone' does not know what attention is, and like the concept of EF, attention is neither easily defined nor easily measured. Any discussion of executive function or working memory necessarily includes references to some kind of attentional system - successful executive functioning requires one to attend, select, and process the necessary information to achieve self-established goals and plans whilst ignoring other sources of information. For example, the proposed model of EF in figure 4, section 3.2 (Anderson, 2002) conceptualises EF as four distinct domains, one of which is attentional control. This is the ability to selectively attend to stimuli, inhibit prepotent responses, and focusing attention for long periods. It also involves regulating and monitoring actions to ensure that goals are achieved. Baddeley's (1986) model of working memory also incorporates an attentional system – the central executive – a system that is responsible for the attentional control of action and has the capacity to focus, divide, and switch attention. Hence, attention is not a single unitary process, nor does it reflect a single, general, cognitive function or mechanism (Posner & Petersen, 1990) but is perhaps better conceptualised as a property of the cognitive system (Cohen, Aston-Jones, & Gilsenrat, 2004).

3.2.1.3. Posner & Petersen's model of attention

A highly influential model of attention was developed by Posner & Petersen (1990). They propose an attention system consisting of three separate subsystems served by distinct anatomical regions: a selection or executive system: a vigilance system, and an orientation system. Posner & Petersen (Posner & Petersen, 1990) argue that different anatomical areas carry out specific cognitive operations. This is supported by evidence

from human patients showing that deficits to the attention system differ depending on the area of the brain that is injured. Imaging studies also support the notion that different attentional subsystems are subserved by distinct anatomical areas (Posner & Peterson, 1990).

3.2.1.4. Shifting

Shifting (or attention switching) is one of three executive functions examined in a latent variable analysis of executive functions by Miyake et al. (2000). It refers to the ability to move flexibly from one cognitive or behavioural strategy to another. Miyake et al. (2000) suggest that shifting not only encompasses the ability to engage and disengage appropriate tasks, but also the ability to perform new operations when faced with proactive interference or negative priming. ERP studies implicate the frontal lobes may regulate this ability (Moulden et al., 1997).

3.2.1.5. Updating

Another EF postulated by Miyake et al. (2000) is the updating and monitoring of working memory representations, and is closely related to the concept of working memory. Updating operates to monitor and code incoming information that is relevant to the task in hand, items held in working memory are then revised or replaced appropriately. Miyake et al. (2000) suggest that a fundamental aspect of this executive function is not simply to passively store information, but to actively manipulate information.

3.2.1.6. Inhibition

According to Barkley (1997) behavioural inhibition is composed of three interrelated processes: (a) inhibition of the initial prepotent response to an event; (b) stopping of an ongoing response, which thereby permits a delay in the decision to respond; and (c) the protection of this period of delay and the self-directed responses that occur within it from disruption by competing events and responses (interference control).

3.3. THE NEUROPSYCHOLOGICAL ORGANISATION OF EXECUTIVE FUNCTIONS

As noted above, two major issues in the study of EF concern how they are related to the frontal lobes and how executive processes are organised – particularly the extent to which different executive processes are separable or unitary. Indeed these two issues are

themselves difficult to separate, as much of the literature examining the unity and diversity of EF do so in the context of examining the frontal lobes, and many authors interchange the use of psychological and anatomical definitions of executive functions and frontal lobe functions. The first part of this section will attempt to give an overview of why executive functions are associated with the frontal lobes, followed by a examination of the 'unity and diversity' of frontal lobe functions.

3.3.1. Executive Function and the Frontal Lobes

Historically, the understanding of executive functions has stemmed from studies of patients with frontal lobe damage who appear to exhibit significant 'executive dysfunction'. In 1868 Harlow described the case of a man (Phineas Gage) who had suffered a frontal lobe lesion following a penetrating head trauma caused by a tamping iron that was blown through his head (Harlow, 1868, in Cato, Delis, Abildskov, & Bigler, 2004). Although Gage survived the accident, severe personality and behavioural changes were observed - a profile that has become associated with frontal lobe syndrome. Subsequent researchers found that patients with lesions to the frontal lobe areas show impairments on a range of executive tasks such as the Wisconsin Card Sorting Test (WCST) and the Tower of Hanoi (ToH). Such early observations of a relationship between higher-order cognitive processes and the frontal lobes are, at least in part, responsible for the early assumption of equivalence between the frontal lobes and executive processes. Many subsequent researchers used the terms "frontal lobe functions" and "executive functions" interchangeably; a practice that has been subject to criticism, with some authors suggesting this association has obstructed the understanding of executive functions (Stuss & Alexander, 2000).

Although most researchers would agree that some kind of relationship exists between EF and the frontal lobes, the nature of this association is currently ambiguous and unspecified. As noted by Stuss & Alexander (2000), there is 'no clinical condition with specific and easily limited relation to the frontal lobes…' Nor is there a large pool of participants with well-defined frontal lesions that would allow the issue of specificity to be addressed. Alexander & Stuss (2000) argue that characterising "frontal functions" is best done at an anatomical level. There are five parallel, but independent, subcortical circuits, that each involve a frontal lobe area. Three of these circuits determine cognitive and affective behaviours, and are associated with distinct cognitive and behavioural profiles following lesions (Alexander & Stuss, 2000). Research examining cognitive

deficits following frontal lobe lesions has not provided conclusive evidence that executive functioning can be localised in the frontal lobes. Whilst many executive deficits are present in patients with frontal lobe lesions, executive dysfunction is also found in patients whose lesions are in areas other than the frontal lobes (Anderson, Damasio, Jones, & Tranel, 1990). Furthermore, some patients with frontal lesions demonstrate intact performance on executive function tasks (Eslinger & Damasio, 1985).

There are several methodological explanations for such findings that are discussed in detail in subsequent sections (see section 3.5) Hence, many authors now argue that the synonymous use of anatomical and functional terms is inappropriate, as the term frontal lobe and executive are not conceptually identical (Alexander & Stuss, 2000; Miyake et al., 2000; Baddelely et al., 1997). Other researchers (Fuster, 1997) oppose attempts to localise cognitive functions in the prefrontal cortex, arguing that executive cognitive functions such as working memory and attention are subserved by the frontal lobes but not localised within that anatomical structure. Fuster (1997) argues that neuronal networks operating within the PFC collaborate with networks from other cerebral structures to provide the basis by which behaviour and speech is organised. This is supported by non-invasive neuroimaging techniques such as MRI (magnetic resonance imaging) and also contradicts the assumption that the concept of EF can be precisely mapped onto the frontal region of the brain. Fuster et al. (1997) found modest support for a relationship between EF and the frontal lobes. They correlated performance on a variety of EF tasks with degree of atrophy in the frontal brain regions of patients with Alzheimer's disease (AD). Few of the executive tests showed true selective association with frontal regional measures, instead the majority of the tests correlated with atrophy in other brain regions.

3.3.2. Executive Function: Unity or Diversity?

Another major issue in the study of EF has been the debate concerning the unity and diversity of the functions of the frontal lobes. This issue was raised by Teuber (1972) and has been subsequently debated by other theorists (Duncan, Johnson, Swales, & Freer, 1997; Miyake et al., 2000). Specifically, if EF is conceptualised as reflecting several different cognitive processes, then to what extent do those various processes reflect a common underlying mechanism? For example, Engle, Kane, & Tuholski (1999) argue that a unitary approach to the working memory and attention system is

most appropriate, although they also admit that the system is unlikely to be entirely unitary. In contrast, others have suggested that the occurrence of dissociated impairment supports the view that executive function is controlled by multiple and separable processes. Godefroy, Cabaret, Petit-Chenal, Pruvo, & Rousseaux (1999) found selective impairments with double dissociations of various processes in a sample of patients with frontal lobe lesions. Rather than use very diverse EF tasks that utilise very different sorts of non-control processes, they selected tasks that were less complex than traditional tasks. They argue this evidence supports fractionation of executive functions in line with both Baddeley (1986) and Stuss & Alexander (2000).

Another approach to examining the unity and diversity of executive functioning is to use correlational or factor-analytic methodology. This entails administering a large battery of executive tests to a number of participants and then examining performance results by using correlational-regression or factor analyses. As noted by Miyake et al. (2000), this methodology has typically produced low correlations (r = .40) with exploratory factor analysis yielding multiple factors in support of the non-unitary nature of executive function. The correlational approach has also been used in studies of patients with frontal lobe lesions, where the correlations between tasks assumed to reflect executive (and therefore frontal) functions are compared to the correlations among non-frontal tests. Unfortunately this has produced conflicting results; some studies have shown positive and substantial correlations among frontal tests, whereas others have shown low correlations among the frontal tests as well as little difference in the correlations between frontal and non-frontal tests (Baddeley, 1997; Miyake et al., 2000). Miyake et al. (2000) examined the relationship between three different executive functions: shifting, updating, and inhibition. The three processes were clearly distinguishable from one another yet moderate correlations between the three factors indicate underlying commonality. Stuss & Alexander (2000) emphasise the non-unitary nature of EF and propose that executive functions should be conceptualised as distinct processes that are related to different regions of the frontal lobes but which are also representative of a general concept of control functions.

3.4. Measuring Executive Function in Adults

Historically, the aim of measuring EF has arisen from the need to identify the neuropsychological deficits experienced by patients who have suffered brain trauma. As

noted above, the story of Phineas Gage demonstrated how severe brain trauma to a particular brain region, can cause very specific deficits. It is, therefore, unsurprising that most tests of EF are developed with the aim of identifying neuropsychological deficits within patient populations. Some of the commonly used measures of adult EF are described below, tests that have been specifically developed for use with children are discussed in section 3.8.

Wisconsin Card Sorting Task

A widely used task that requires participants to match test cards to reference cards according to the colour, shape, or number of stimuli on the cards. Feedback is provided after each match, enabling the participant to acquire the correct rule of classification. After a fixed number of correct matches, the rule is changed without notice and the subject must shift to a new mode of classification. It is believed that the WCST measures cognitive flexibility, the ability to alter a behavioural response mode in the face of changing contingencies. Patients with lesions to the prefrontal cortex often show deficits in WCST performance.

Stroop

The classic Stroop task presents participants with three conditions consisting of lists of colour words and participants have to read aloud the colour of the ink in which the word is printed. Trials usually consist of reading colour words printed in black, naming colour patches, and naming the colour of ink in which the colour word in printed in. Congruent trials occur where the word and the ink colour match. Incongruent trials occur when the word and the colour ink are different, e.g. the word ‘red’ printed in the colour green. It is this condition that typically elicits the ‘Stroop’ effect, a significant slowing of performance. The Stroop test is commonly used as a test of inhibition.

Verbal Fluency

Sometime referred to as letter fluency (Phillips, 1997 in Burgess, 1997), this test requires participants to generate as many words as they can, beginning with a specified letter in a set time period.

Tower of Hanoi/Tower of London

The Tower of Hanoi (ToH) consists of three pegs and four disks of differing sizes. The discs have holes so they can be stacked on the pegs. The disks can be moved from one

peg to another. Only the top disk on a peg can be moved, and it can never be placed on a smaller disk. The discs all start out on one peg, but the goal is to move them all to the third peg, one disk at a time, by means of transferring disks among pegs. The Tower of London (ToL) has been developed and used as an alternative to the ToH (Shallice, 1982). Like the ToH, the goal is to rearrange three objects (coloured balls) on three pegs. Three different coloured balls are arranged on three pegs of descending length that can hold 3,2, and 1 balls respectively. Only one ball can be moved at a time, and the difficulty of the task can be graded depending on the end state that is required and the minimum number of moves required to accomplish the end state.

3.5. Methodological Issues In Measuring Executive Functions

The following sections shall attempt to address the many methodological issues in measuring executive functions. These include issues of reliability and validity and issues of task impurity. The very nature of EF - higher-order cognitive processing - means that traditional tasks developed to assess EF in adults are complex and designed to be difficult. Tapping into the numerous processes thought to underlie EF requires a task that engages a number of cognitive processes at the same time. Hence, any EF task may require the performance of several distinct underlying processes, as well as other non-executive processes. Furthermore, executive tasks are also subject to criticism regarding the low correspondence between process and behaviour. Executive processes typically manifest themselves in a wide variety of situations, rather than many psychological processes, which only manifest themselves in one type of situation. Burgess (Burgess, 1997 in Rabbit) gives an example of the face recognition system being activated only when a participant is shown a face, whereas it is not activated when a participant is shown a list of words. In contrast, an executive process like working memory will be used in many different situations.

In addition to methodological issues in measuring executive function there are also conceptual issues. As noted above, a key problem in the study of executive processes has been the lack of any operational definition of EF. As such, there is no precise experimental manipulation or screening measure to study these processes and attempts to characterise executive dysfunction has been severely constrained by the lack of any one specific test that is failed by all patients assumed to be dysexecutive (such as frontal

lobe patients) and the ability of some dysexecutive patients to accurately perform particular EF tests.

3.5.1. Repeated Testing

A key feature in most descriptions of EF is the assumption that EF operates in only novel situations. Theorists often use the distinction between controlled and automatic processes when discussing executive and non-executive processes (Hughes & Graham, 2002). Over time, controlled actions may become automated as a consequence of frequent repetition, and therefore no longer under the control of EF. As such, specific tasks developed to assess EF can only be administered once to a participant. Repeated testing of the same task with a participant is unlikely to produce similar results and will be less reflective of underlying executive processes. A fundamental assumption in experimental psychology concerns the ability of test instrument to consistently measure whatever it purports to measure. Hence, if a test is assumed a good measure, then it should produce similar results across different testing situations. Inconsistent results reflect measurement error and are often attributed to chance factors such as differences in motivation from one time to another. A task can only be considered novel on the first occasion it is administered, consequently, the test/retest reliability of EF tasks can be low (Rabbitt, 1997).

3.5.2. Issues of Task Complexity

EF tasks are necessarily complex. They are designed to be difficult, as they must tap higher-order cognitive processes thought to underlie executive functioning. Such complexity, however, is a multiple source of measurement error. Most, if not all, executive tasks will activate non-executive processes that may be unrelated to the task, or may in fact be necessary for accurate performance. Hence, any task performance measure will also reflect the performance of non-executive processes. Such task impurity is argued to be a high degree of measurement error in executive tasks (Burgess, 1997). The complexity of EF tasks is also an issue when attempting to differentiate between the performance of distinct executive processes. Many EF tasks require the execution of several processes thought to underlie executive functioning, hence task scores will be a product of various executive processes pooled together (Hughes & Graham, 2002).

3.5.3. The Relationship between Process and Behaviour

Another methodological issue concerns the apparent lack of correspondence between process and behaviour in executive functioning. Unlike many psychological processes that manifest themselves in only one situation, executive processes manifest themselves in a range of different situations. Hence, any particular executive task will elicit a range of behaviours, such as planning, memory, and attention. Burgess (1997, pg85) offers a good example of facial expression processing. The cognitive process involved to judge facial emotion from a photograph is highly dedicated to supporting behaviour in that situation. Whereas the cognitive processes underlying executive functioning are activated in numerous different situations.

3.5.4. Cognitive Congruence

A major issue for EF theorists concerns the finding that performance on virtually any cognitive task will positively correlate with performance on any other cognitive task. This notion of cognitive congruence is fundamental to the concept of general intelligence (g) and some theorists have argued that g and EF should be considered parallel, with g reflecting frontal lobe processing (Duncan, Emslie, Williams, Johnson, & Freer, 1996). If one assumes the viewpoint that g and EF do not reflect the same process, cognitive congruence can pose a problem when examining the relationship between performance measures from EF tasks. Scores from EF tasks will naturally be positively correlated, based on the phenomena of cognitive congruence. The difficulty lies in determining whether any of the relationship is due to shared EF processing, rather than simply a reflection of g. Burgess (1997) argues that the relationship between EF measures cannot be explained by cognitive congruence alone.

3.6. Developmental Aspects of Executive Function

An aim of this thesis is to examine EF in children; hence the following sections will examine EF in more detail but specifically in relation to developmental aspects of EF. In comparison to the adult literature, there is a paucity of studies examining EF in children. According to Hughes (2002, p. 202) the “chronic neglect” of developmental changes in executive functions is due in part to the assumption that the PFC, the assumed location of EF, did not fully mature until adolescence, and also the lack of developmentally appropriate tasks. Although this attitude towards EF research in children has diminished, there are still significant gaps in the literature. For instance,

one of the key texts in the area of EF research makes no mention of the specific issues when measuring EF in children (Methodology of Frontal and Executive Function, Rabbitt, 1997).

Unfortunately, the same conceptual and methodological issues that have plagued EF research with adults have also hampered investigations of EF in children. These include conceptual issues in defining EF; the relationship between EF and the frontal lobes; issues of unity and diversity; and methodological issues such as task complexity and impurity. In addition, researchers have also been faced with new methodological dilemmas specific to research with children that are a consequence of qualitative and quantitative differences between adult and child cognition, and in particular, language abilities. In addition, the influence of brain maturation upon executive functioning also poses difficulty for researchers. As discussed in Chapter 2, frontal areas of the brain are known to develop much later than other brain structures and researchers have yet to identify how this issue influences the development of EF.

The following sections shall firstly examine the additional methodological issues facing EF research with children. Next, I shall examine various attempts at developing (or adapting) tasks that are developmentally appropriate for children of various ages. Finally, I shall consider how maturation of the brain may influence the possible developmental trajectory of EF.

3.7. Assessment of Executive Function in Children: Methodological Issues

3.7.1. Repeated Testing

Hughes & Graham (2002) argue that some of the methodological issues in adult EF research may not apply to children. As noted above, a key problem with adult research concerns the restriction on repeated testing. However, if one presumes that the shift from controlled to automatic processing is extended in children compared to adults; repeated administration of a task should be processed as novel despite previous testing. Hence, test/retest reliability may be stronger in children compared to adults. However, brain maturation is continually occurring in a child, and depending on the time frame

between the initial and subsequent tests, a child's brain may have undergone significant maturational changes that enhance the child's ability to complete the task.

3.7.2. Task Difficulty

Due to the very nature of EF – as higher-order cognitive processing – traditional tasks designed to tap executive function in adults were naturally designed to be complex and difficult, executive functioning is not supposed to be easy! Hence, the main obstacle for measuring EF in children concerns the fact that most executive function tasks are simply too difficult for many children. Difficulty may arise due to the absolute level of cognitive ability required to perform the task, or it may be due to other requirements of the task, not necessarily concerned with executive processes. A commonly cited problem with EF tasks is their reliance on language skills. Standard executive function tasks are not appropriate for children due to their complexity and must be simplified; consequently, there is less likelihood of non-executive processes being triggered during the task. This simplification of executive function tasks, enables processes to be examined in isolation, rather than simultaneously tapping several processes. Hence, the issue of 'task impurity', discussed above, may be less of a problem in developmental research (Hughes & Graham, 2002).

3.7.3. Language Issues

Although language ability varies as function of age, younger children in particular may have quite limited language ability that could have several adverse effects. Firstly, language may be necessary to understand the researcher's instructions; it may not be always possible to simplify instructions to make them easily understood by children. Secondly, some executive function tasks will require verbal comprehension, as noted above, performance on any given executive function task will be influenced by non-executive processes that are also triggered during testing. Hence, if a task requires a level of verbal comprehension above that of the child, the scores from that child's performance will be a reflection of verbal comprehension rather than EF.

A second language-related problem concerns the automaticity of Verbal Fluency. For most adults, reading and speaking words can be considered automatic processes. Several EF tasks that are used with adults rely on the assumption that these skills are automatic. For instance, the 'Stroop' task is used to measure the ability to inhibit a

prepotent response, reading the word, and instead read the ink colour that the word has been written in. As Hughes & Graham (2002) highlight, fluent literacy emerges late in childhood hence such tasks may be developmentally appropriate for children.

A third language-related problem is one that has been extensively discussed by Zelazo et al. (Zelazo & Muller, 2002; Zelazo, Muller, Frye, & Marcovitch, 2003) who argue that language is crucial for children's ability to control and guide their actions. The Cognitive Complexity and Control (CCC) theory offers a comprehensive account of age-related changes in the ability to control and guide one's actions. According to the CCC theory, the acquisition of language enables children to use silent self-directed speech in the form of "if-then" rules to control behaviour. As children get older, the complexity of the rules that children are able to formulate increases, enabling the formulation of solutions that are also greater in complexity. At about two and a half years old, children can represent a single explicit rule such as 'if A, do X'. By 3 years of age children can consider two rules simultaneously but they are unintegrated, such as 'if A, do X, if B do X'. By around four or five, children then start to represent higher-order relations and can integrate two incompatible rules, such as 'if A, do X, if B do X, but, if A and B do Y'. Zelazo's theories were heavily influenced by early developmentalists such as Vygotsky and Luria, who proposed that the development of inner speech, or internal verbalization, enables actions and behaviour to be planned, coordinated, and regulated. I shall return to Zelazo's CCC theory when discussing theories regarding the development trajectory of EF.

3.8. Executive Function Tasks for Children

Several tasks designed to measure EF in adults have been successfully used to measure EF in children. However, the use of tests developed and validated for adult populations has been criticised as having questionable validity (Anderson, 2002). Adult tasks that have been used with children include the WCST, as described in section 3.4.1.1, which has been used with children aged from 6- 12-years (Chelune & Baer, 1986) and the Tower of Hanoi (Welsh, Pennington, & Groisser, 1991). A comprehensive account of earlier EF tests used in children is given by Anderson (2001) who also suggests that EF emerges at around the age of six. Recently, however, there has been a surge of interest in examining executive functioning before the age of six, and, in particular, preschool children.

3.8.1. Preschool Children

There is a particular clinical interest in examining EF in younger children. Several developmental disorders that are characterised by deficits in executive functioning manifest themselves during childhood. Children with ADHD typically have difficulties with sustained attention, hyperactivity, and impulsivity. Various theories have been proposed to account for the disorder; in particular Barkley (1997) argues that ADHD should be considered a disorder of executive functioning. Impairments in EF have also been demonstrated in autism, babies born prematurely, and genetic disorders. Hence, it is essential that EF can be measured in such diverse clinical populations using instruments that are reliable and valid.

Espy et al. (Espy, Kaufmann, Glisky, & McDiarmid, 2001; Espy, Kaufmann, McDiarmid, & Glisky, 1999) have successfully adapted several neuropsychological tests from the literature to enable their use with preschool children. Rather than decreasing task demands of adult tests, Espy, Kaufman, McDiarmuid, & Glisky (Espy et al., 1999) measured EF in children by increasing the task demands of the A-not-B test, originally used to investigate infants knowledge of objects (object permanence) by Piaget (1954) and extensively adapted and used by researchers since (Baillargeon, Graber, Devos, & Black, 1990; Diamond, 1988; Matthews, Ellis, & Nelson, 1996). The original task requires infants to observe and then retrieve a reward hidden in one location (A). After several trials, the hiding place of the reward is moved to a second location (B). Typically, infants below 12 months demonstrate perseveration and continue to search for the reward in location A, despite having witnessed the object hidden in location B. In a study of preschoolers aged 23-66 months, Espy et al. (1999) included more than one reversal trial and a 10-second delay between hiding and retrieving the object. They found age-related improvements on the task and argue that their results support the existence of both working memory and inhibition processes in very young children. More recently, the A-not-B (AB) task has been proposed to represent an early manifestation of executive functioning (Espy et al., 1999) based on its similarity to the delayed response paradigm (used in the animal neuroscience literature), successful performance of which is related to frontal lobe maturation (Diamond & Doar, 1989).

Following on from this study Espy et al. (2001) employed a variety of procedures to successfully assess EF in preschool children. One example is the “shape school” - a task

designed specifically for use with young children that is a visual adaptation of the Stroop task described above. The child is presented with characters of different colours and shapes in a storybook format. In the control condition, the child has to name as fast as possible the names of the characters, the child is told that the name of a character is their colour - this establishes a prepotent response bias to name the stimulus colour. Then in the inhibit condition, the figures presented have either a happy (ready for lunch) or sad face (not ready for lunch), and the child must name, as fast as possible, the figure colour of those pupils who are ready for lunch. Espy et al. (2001) found age-related increases in performance on many of these tasks demonstrating the capacity these tasks have to measure EF in very young children.

Similarly, Bull, Espy, & Senn (2004) demonstrated that not all adult EF tasks are unsuitable for use with preschool children. Children aged from 3 to 6 years were tested on two EF tasks used extensively with adults: the Tower of Hanoi (ToH) and its variant the Tower of London (ToL). The ToH presents the child a model comprised of three equal-sized pegs (described to the child as 'trees') and three different coloured rings ('baby, mommy, and daddy monkey'). The pegs are graduated so that the rings will only fit on the pegs stacked from largest to smallest. The goal is to "bring the monkeys home to sleep on their tree". To do this, the child must move the three rings, one at a time, among the pegs to achieve the configuration shown on a second model. Different starting configurations will result in progressively more difficult problems, by increasing the number of moves required to achieve the end-state. Their results successfully demonstrated the use of inhibition and shifting, or mental flexibility, by preschool children.

3.8.2. School-Aged Children

More recently, new methods to assess EF have been developed that are gaining acceptance as valid and reliable instruments. A brief overview of some key measures is given below.

3.8.2.1. NEPSY

The NEPSY (Korkman, Kirk, & Kemp, 1998) is a developmental neuropsychological assessment battery for use with children aged 5-12 years. It consists of 27 subtests divided into five functional domains: attention and EF; language; sensorimotor; visual-spatial; and memory and learning. In developing the assessment battery, the authors applied Luria's theories and principles of cognitive processes as dynamic functional systems with specific aims, yet carried out by a system of interconnected subprocesses.

3.8.2.2. Test of Everyday Attention for children (TEA-Ch)

The TEA-Ch (Manly, Robertson, Anderson, & Nimmo-Smith, 1999) is a children's version of the Test of Everyday Attention, a standardised neuropsychological test battery designed to evaluate attentional capacity. The development of the original Test of Everyday Attention (for adults) was based on the model of attention by Posner & Peterson (1990). As described earlier, the model posits three separate attention systems – executive, selection, and vigilance. The TEA-Ch includes subtests designed to assess the selection and vigilance systems identified Posner and Petersons model. In designing the TEA-Ch, the authors attempted to address many of the methodological issues that surround assessment of executive functions in children. For instance, language requirements are kept to a minimum and some tasks control for motor speed. The TEA-Ch that has been successfully used to measure attentional processes in children aged 6-16 years (Manly et al., 2001). It consists of nine subtests that are posited to assess selective attention, attentional control, and sustained attention.

3.8.2.3. CANTAB

The Cambridge Automated Neuropsychological Testing Battery (CANTAB) is a computer administered cognitive assessment tool designed to assess neuropsychological functioning associated with the frontal lobes such as memory, visual attention, planning, visual memory, and working memory. It was originally developed for use with normal elderly populations and brain-damaged patients. The CANTAB was developed about 15 years ago and has since been used in a number of studies, with standardised and validated normative data available for ages 4 - 90 years of age (Luciana & Nelson, 1998). CANTAB tests also have satisfactory levels of test re-test reliability. Neuro-imaging studies have confirmed the neuro-anatomical basis of the tests. The CANTAB is ideal for use with children for a number of reasons: 1) All task stimuli are nonverbal

thus reducing any potential performance differences due to language ability; 2) It can be used with children for whom English is not their first language; and 3) Children find the computerised testing format to be interesting and motivating (Luciana, 2003). The CANTAB in its most recent form consists of 22 subtests and touch-screen technology is used to enable rapid and accurate processing of responses.

3.8.2.4. Behavior Rating Inventory of Executive Function

The Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000) is a relatively new inventory that has been developed to measure executive dysfunction in children aged 5-18 years using parent and teacher reports. As well as an overall score, the questionnaire fractionates EF into two broad domains: Behavioral Regulation and metacognitive ability. These two domains are further fractionated into a number of different elements such as working memory, inhibition, shifting, and planning.

3.9. THE DEVELOPMENT OF EXECUTIVE FUNCTION DURING CHILDHOOD

A major issue for researchers examining EF in children concerns the development of cognitive functions. Many cognitive skills develop in an irregular and rapid pattern throughout childhood making it difficult to map the development of these processes. As noted above, early theorists assumed that EF did not emerge until around the age of twelve years, this was based on the assumption that the frontal lobes were not functionally mature until around this age but neuroimaging studies have refuted this assumption, illustrating prefrontal activity in infancy (Bell & Fox, 1992). In addition, many studies have demonstrated age related changes on many EF tasks suggesting that as the frontal lobes mature, executive functioning becomes more effective. A brief overview of research to-date is given below.

Diamond & Taylor (Diamond & Taylor, 1996) used the 'tapping test' developed by Luria, who was a prominent frontal lobe researcher in the 1960's. This task requires the ability to hold two things in mind and to exercise inhibitory control over one's behaviour. Luria (1966, in Diamond & Taylor, 1996) found that patients with frontal lobe damage have difficulty in performing this task. Participants are required to tap once when the experimenter taps twice, and to tap twice when the experimenter taps once. As a relatively simple and straightforward task, it is ideal for use with children.

Diamond & Taylor (1996) found age-related improvements in performance between the ages of four and seven years, they initially included three-year-old children but the task was too difficult for that age. Diamond & Taylor (1996) propose that between the ages of three and seven years, important changes in executive control are occurring that may reflect significant changes within the frontal cortex.

Recent research by Espy et al. (2001) has also demonstrated age-related changes in executive functioning in preschoolers. A battery of tasks measuring inhibition, working memory, cognitive flexibility, and planning was administered to children aged between 30 and 60 months. Performance on many of the tasks was related to age and largely independent of intelligence or gender.

Reviewing the evidence, Anderson (2002) argues that different executive processes have different developmental trajectories and mature at different rates. Some researchers argue that most executive processes come 'online' at about the age of eight (Luciana & Nelson, 1998). Improvements in executive functioning has been associated with increased myelination of prefrontal connections, which is proposed to improve executive functioning by enhancing the integration of cognitive processes and improving the processing of information (Anderson, 2002).

3.9.1. Processing Speed

Underlying many aspects of cognitive development is the speed with which basic cognitive processes are executed. Conceptualised as a general, task-independent construct (Fry & Hale, 2000), research has clearly demonstrated that processing speed reliably predicts performance on a range of cognitive tasks. A consistent pattern of age related changes in processing speed has been demonstrated, showing that the speed with which children process information increases exponentially from early childhood to adolescence (Hale, 1990). Kail (1991) argues that a single global mechanism is responsible for the developmental course of processing speed and age-related decreases in processing time reflect an increase in the processing resources that can be allocated to the task (Fry & Hale, 2000). Processing speed has been related to working memory performance (Fry & Hale, 1996) and independently predicts children's ability to solve word-problems (Kail & Hall, 1999). Although processing speed is not an executive function, it clearly has important implications for the development of children's executive functioning and performance on EF tasks.

3.10. CHAPTER SUMMARY

Executive functions are clearly fundamental to children's development. However, our understanding of the development of EF in childhood is still in its infancy, and research has yet to elucidate all the factors that may negatively affect EF development. Development of EF appears to be related to maturation of the frontal lobes (particularly the PFC), an area of the brain, which as noted in Chapter 2, is thought to derive particular benefit from sleep-related restorative processes. This theory raises questions about the vulnerability of a child's brain when asleep. If the PFC is particularly vulnerable to the effects of sleep disturbance, does this mean that a lack of sleep, or disrupted sleep may affect the long-term development of EF in children? Alternatively, plasticity of the developing brain in its early years may afford some protection from any permanent damage to the PFC and subsequently executive functioning.

The following chapter examines whether children with respiratory disease are at risk of sleep disturbance and consequently whether they are also at risk of neuropsychological deficits that have been associated with sleep disturbance.

CHAPTER 4 SLEEP IN CHILDREN WITH RESPIRATORY DISEASE

4.1. INTRODUCTION

The brain is particularly vulnerable to sleep related changes in the respiratory system, which can impede the continuous supply of oxygen, upon which the brain is intrinsically dependent. In normal healthy adults and children, several changes to the respiratory system occur during sleep: decreased minute ventilation, increased upper airway resistance, and decreased ventilatory drive. Hence breathing is impaired during normal sleep, and particularly during REM sleep (Marcus, 2001). These sleep-induced changes to the respiratory system are exacerbated in children with certain predisposing factors causing sleep-disordered breathing. Children with pre-existing respiratory problems are likely to be at risk of neuropsychological deficits from multiple pathways – the effects of hypoxia on the immature brain and the effects of sleep fragmentation on the prefrontal cortex. This chapter will examine whether children with respiratory disease may be at risk of sleep disturbance, and consequently the neuropsychological deficits that have associated with sleep disturbance as discussed in Chapter 2. Specifically this chapter will focus on the effects of cystic fibrosis on children's sleep but will begin with a brief overview of the effects of asthma on children's sleep.

4.2. ASTHMA

Asthma is an inflammatory condition of the airways that is reported to be the most frequent chronic disease of childhood (Roder, Kroonenberg, & Boekaerts, 2003). An estimated 1.1 million children in the UK are receiving treatment for the disease (Asthma UK) and the UK is reported to be one of the worst countries affected by increased prevalence rates (Kurukulaaratchy, Fenn, Twiselton, Matthews, & Arshad, 2002). In addition to the medical symptoms experienced by asthma sufferers, such as coughing, wheezing, shortness of breath and tightness in the chest, children are also at risk of a variety of emotional and social problems (McCann et al., 2002). School attendance of children with asthma is worse compared to children without asthma (Roder et al., 2003). High prevalence of emotional and behavioural problems has also been reported in children with asthma (Calam, Gregg, & Goodman, 2005).

4.2.1. Sleep Disturbance in Asthma

Asthma symptoms typically worsen at night and such nocturnal symptoms are associated with increased morbidity and mortality (Strunk, Sternberg, Bacharier, & Szefler, 2002). An epidemiological survey found that 74% of participants experienced night-time awakenings, difficulty in maintaining sleep, and daytime sleepiness (Turner-Warwick, 1988). An association has also been documented between sleep-disordered breathing and asthma with the suggestion that a dual causal relationship may exist between nocturnal asthma and SDB (Bohadana, Hannhart, & Teculescu, 2002).

4.2.2. Studies of Childhood Asthma and Sleep Disturbance

A large-scale study of children enrolled in a randomised clinical trial of treatment for mild-moderate childhood asthma screened over 1000 patients for 28 days (Strunk et al., 2002). Approximately one third (33.7%) of the children experienced 1 or more night wakings and 13.7% reported 3 or more awakenings. The risk of nocturnal awakenings was increased if the child's asthma symptoms were more severe. The presence of atopy, as determined by a skin-prick test, also increased the risk of night-time awakenings. A major weakness of this study was the lack of any comparisons with non-asthmatic children.

In contrast, Ronchetti et al (2002) did not find a relationship between childhood asthma and sleep disturbance. This was an epidemiological study aimed at evaluating whether any extra-respiratory symptoms, such as behavioural changes, are associated with asthma. Sleep disturbance was measured using a parental response to the question 'is your child affected by disturbed sleep?' There were no significant differences between children with and without asthma symptoms. Although this was a large-scale study using over 1000 children, there were no objective measurements, either of asthma symptoms or of sleep disturbance. Furthermore, the use of a single question to ascertain the presence of sleep disturbance is methodologically questionable.

Desager, Nelen, & De Backer (2005) also used a large cross sectional population of approximately 1000 school-aged children to investigate the relationship between wheezing symptoms and sleep disturbance. Children with wheezing symptoms (8.8% of the sample) were two times more at risk of having difficulty falling asleep and 5 times more at risk of restless sleep and daytime tiredness. They were also more likely to report symptoms of snoring and nocturnal awakenings compared to children with no

wheezing symptoms. Although this study did not include objective measures of sleep disturbance, asthma symptoms were assessed using various pulmonary function tests. In addition, sleep disturbance was assessed using seven questions rather than the single question used by Ronchetti et al. (2002).

One study has used objective measures of sleep disturbance to assess asthma symptoms in children. Sadeh, Horowitz, Wolach-Benodis, & Wolach (1998) monitored 40 asthmatic children (mean age was 12 years) and 34 healthy controls with wrist actigraphs, and assessed asthma symptoms using peak-flow meters, for three days. Neither sleep duration, nor sleep percent[2] were significantly different between asthmatics and healthy controls. However, quiet sleep[3] was significantly reduced and mean activity level significantly increased in asthmatic children. Sleep percent was correlated with peak flow measures in the whole sample but not in the asthmatic children alone. Mean activity level was significantly correlated with morning and evening peak-flow measures in asthmatic children only. Lower peak-flow measures were associated with poorer sleep. The authors suggest that asthmatic children may be at risk for developing neuropsychological deficits associated with sleep loss.

As noted above, an association between asthma symptoms and SDB has been well-documented in the adult population. Redline et al. (1999) explored this association in an epidemiological study of 399 children. Overnight home polysomnography was performed to determine the presence of SDB. Children with clinically diagnosed asthma were almost four times more at risk of SDB compared to non-asthmatic children. In addition, both occasional wheeze and persistent wheeze strongly predicted SDB (adjusted odds ratio, 3.29 and 7.45 respectively).

4.2.3. Neuropsychological Deficits Associated with Asthma

As noted above (Sadeh et al., 1998), it has been suggested that childhood asthma may be a risk factor for neuropsychological difficulties that have been associated with sleep disturbance such as decreased attention (Sadeh et al., 2003) and poorer working memory performance (Steenari et al., 2003). The evidence regarding a possible neuropsychological dysfunction in children with asthma is limited.

[2] Sleep percent: percent of actual sleep time from sleep duration (excluding wakefulness after sleep onset

[3] Quiet sleep: percentage of sleep without any motion

A large-scale clinical trial assessing the effectiveness of two drug treatments for childhood asthma also measured neurocognitive functioning (Annett et al., 2000). A battery of tests were administered to children that included the Weschler Intelligence Scales (WISC), the Woodcock-Johnson psychoeducational battery, the Wide Range of Memory and Learning (WRAL), and the Gordon Diagnostic Systems (GDS). Compared to normative data from the neurocognitive tests, children with mild-moderate asthma did not show any increased difficulties although there was a trend for asthmatic children scoring lower on tests of vigilance and distractibility. In addition, there was no relationship between asthma severity and academic competence.

A comprehensive review undertaken by Milton, Whitehead, Holland, & Hamilton (2004) examined the social and economic consequences of childhood asthma, which included school attendance and academic achievement. They concluded that although children with asthma have more days off school compared to their healthy peers, this did not manifest as poorer performance at school. For instance, Silverstein et al. (2001) compared 92 children with asthma to age and sex matched controls and found that children with asthma had on average 2.2 more days off school. A comparison of standardised school assessment scores showed no significant differences between the two groups on reading, language, and mathematics. Despite the lack of evidence regarding poorer school achievement, Milton et al. (2004) concluded that children with asthma are at risk for employment problems later in life. It is possible that any neurocognitive deficits experienced by children with asthma are not identifiable by examining school performance in isolation from other markers of cognitive ability.

A search of the literature has uncovered only one study examining sleep, allergy, and neurocognition in children. Stores, Ellis, Wiggs, Crawford, & Thomson (1998) compared neurocognitive functioning in children with asthma to that of healthy control children. Sleep disturbance was measured using overnight home polysomnography and parental report. Cognitive functioning tests measured visuo-motor coordination, memory (short term, auditory, immediate, and delayed recall), and attention. Compared to controls, children with asthma performed significantly worse on the test of delayed recall memory, no other significant differences were found on the cognitive tests. Following treatment for the asthma symptoms performance on some cognitive tasks was significantly improved. In addition, post-treatment sleep measures did not show a

significant improvement in sleep efficiency, although the number of night wakings lasting more than 2 minutes significantly decreased.

4.2.3.1. Summary of sleep and asthma research

In summary, the research examining sleep disturbance and neuropsychological functioning in children with asthma is sparse and inconclusive. However, the limited research indicates that children with asthma may be at risk of sleep disturbance and hence the neuropsychological deficits associated with sleep disturbance.

4.3. CYSTIC FIBROSIS

Children with cystic fibrosis (CF) are proposed to be at greater risk from sleep disturbance due to respiratory problems. Few studies have examined sleep disruption in this population, and to my knowledge no studies have examined whether children with CF are at risk of neurocognitive deficits associated with sleep disturbance and/or sleep related hypoxia.

4.3.1. Background to Cystic Fibrosis

Cystic fibrosis is the most common fatal, autosomal recessive disorder in the UK affecting over 7500 children and young adults. An abnormal membrane based chloride ion channel 'the cystic fibrosis transmembrane conductance regulator' results in abnormal mucous secretions. CF is a multi-system disease but the principle difficulties arise from involvement of the lungs and exocrine pancreas. Abnormal airway surface liquid results in recurrent lower respiratory tract infections, airway inflammation and ultimately bronchiectatic remodeling of the airway. The consequences include increased airway resistance, gas trapping and ventilation-perfusion mismatch. Average life expectancy is currently 31 years (www.cftrust.org.uk) with death most commonly caused by respiratory failure. Exocrine pancreatic insufficiency results in difficulty absorbing nutrients from the gut and failure to thrive in childhood. Relevant to sleep, CF is also associated with nasal polyps and obstruction increasing the likelihood of upper airway obstruction in sleep. Treatment of the disease involves a multicomponent regimen, including airway clearance techniques, aerosol medications, inhalers, pancreatic enzymes, increased calorie intake, and antibiotics.

4.3.2. Sleep Disturbance and Cystic Fibrosis

The progressive underlying lung disease predisposes patients with CF to hypoxemia, which has been associated with sleep disruption in other models of chronic respiratory disease such as obstructive sleep apnoea. Several factors can disrupt the sleep process in CF patients such as nocturnal hypoxia, hypoventilation, chronic cough, chronic inflammation, and medication effects (Dancey, Tullis, Heslegrave, Thornley, & Hanly, 2002). The following section reviews research examining sleep in patients with CF. Although patients with CF are at risk from sleep disturbance, the data are somewhat conflicting. The majority of studies have examined adult patients, with very limited studies examining paediatric patients. Furthermore, despite the known association between disturbed sleep and impaired neurocognitive function, few studies have examined whether patients with CF are at risk of neurocognitive impairment.

4.3.2.1. Adult studies

Impaired neurocognitive function and daytime sleepiness has been demonstrated in adult patients with CF (Dancey et al., 2002). Nineteen CF patients with stable severe lung disease (defined as significant airflow limitation) and 10 age matched control participants underwent overnight polysomnography and assessment of neurocognitive function. CF patients had significantly reduced total sleep time and sleep efficiency compared to controls. The CF group performed significantly lower on most of the neurocognitive tasks compared to the controls. Nocturnal oxygenation was associated with sleep efficiency but not with neurocognitive function.

Sleep and neurobehavioural function has also been examined in adult CF patients experiencing pulmonary exacerbations, compared to clinically stable CF patients (Dobbin, Bartlett, Melehan, Grunstein, & Bye, 2005). Patients with exacerbations had greater sleep disturbance (more time awake after sleep-onset and reduced REM sleep) compared to stable patients. Treatment of the exacerbation was associated with significant improvements in neurobehavioural function. Lung function and total sleep time were correlated in patients experiencing an exacerbation but there was no association between lung function and performance on cognitive tasks.

In contrast, Bradley et al. (1999) found no differences between CF patients and controls in sleep efficiency, arousal frequency or sleep architecture. Likewise, a study comparing sleep, as measured using actigraphy, of CF patients and healthy controls did not find

significant difference in sleep time and sleep efficiency (Jankelowitz et al., 2005). However, they did find that sleep in CF patients was significantly more fragmented, with more night-to-night variability compared to controls.

4.3.2.2. Paediatric studies

Although the majority of published studies examine adult patients with CF, there are a few studies that have examined sleep disturbance in children with CF. A search of the literature did not reveal any studies examining sleep and neurocognitive function in children with CF.

Sleep disturbance has been measured using actigraphy in paediatric CF patients with mild-to-moderate airway obstruction (Amin, Bean, Burklow, & Jeffries, 2005). Forty-four children aged 8 – 18 years and 40 healthy controls completed 5 days of actigraphy. Children with CF had significantly lower sleep efficiency and more frequent awakenings compared to controls. Sleep duration was lower in CF children although this failed to reach significance. Sleep efficiency and sleep duration were correlated with disease severity (as measured using lung function). The age range in this study was very broad and limits generalisations to other samples. Although the average age between the samples was not significantly different, averaging sleep time across a sample comprising children aged 8 years and those aged 18 years can not accurately capture differences in sleep.

Overnight polysomnography has been conducted on 24 children with CF free from acute pulmonary infection (Naqvi, Sotelo, Murry, & Simakajornboon, 2008). Sleep efficiency was significantly decreased in patients with CF compared to healthy controls. Sleep latency did not differ between the two groups, but the percentage of REM sleep was significantly lower in the CF group. Furthermore, severity of lung disease (as determined by lung function) was significantly correlated with the degree of sleep disruption as indicated by sleep efficiency. However, sleep efficiency was not directly correlated with nocturnal hypoxemia or hypoventilation. The authors do not report whether sleep duration or total sleep time differed between the two groups. Furthermore, although the average age of the two groups was not statistically different, the CF mean age was 14.2 and the control mean age was 10.7. From a sleep research perspective, these two ages are developmentally different as the CF group being older, are more likely to have pubertal influences upon their sleep patterns.

In summary, although the research examining sleep disturbance in children with CF is limited, children with CF appear to be at risk of sleep disruption. As reviewed in Chapter 2, there is large body of literature indicating that sleep disturbance is associated with specific cognitive and behavioural deficits, hence there is a need to establish whether children with CF are also at risk of neurocognitive and/or behavioural impairment associated with sleep disturbance.

4.4. Chapter Summary

The literature presented above shows that children with respiratory disease are at risk of sleep disturbance from nocturnal symptoms such as wheezing, night-time cough and SDB symptoms. Children with asthma have been shown to have sleep problems and researchers have suggested they may be at risk of cognitive deficits associated with sleep disturbance. Children with CF can have symptoms similar to children with asthma (nocturnal cough, wheezing, and hypoxia) and studies have suggested that children with CF may suffer from sleep disturbance. There is a growing body of literature demonstrating that children with sleep disturbance are at risk of neuropsychological deficits, related to sleep disruption/ disturbance. Despite this evidence, it is surprising that there is a paucity of literature examining whether children at risk of sleep disturbance due to diseases that affect night-time sleep, are also at risk of the neuropsychological deficits that have been associated with sleep problems. This thesis attempts to address this issue and enhance the current literature by examining sleep disturbance and neuropsychological functioning in children with CF: a research question that to the best of my knowledge has yet to be addressed. The first two empirical chapters address whether EF deficits are associated with sleep disturbance in typically developing children. The subsequent chapters examine whether children with CF are at risk of sleep disturbance and hence neuropsychological deficits that have been associated with sleep disturbance.

4.5. THESIS AIMS AND OBJECTIVES

The studies presented in this thesis aim to explore the relationship between sleep disturbance. cognition and behaviour. Based on the findings presented in section 2.6.1, the thesis incorporates a multi-method design to measure both subjective reports of sleep as well as collecting objective data through the use of actigraphy. The use of a parental questionnaire allows the measurement of more chronic sleep habits, although is subject to error as parents are less likely to be aware of sleep disturbances throughout the night when they are also asleep (or should be!), hence they may not be able to fully comment upon night wakings in their child. As such, the addition of an objective sleep measure was deemed important, and actigraphy the most obvious choice due to the high cost of polysomnography, and the ability of actigraphy to measure over several days in the child's natural environment. Pulse oximetry is also introduced into the methods in Study 2, which provides objective measurement of night-time oxygen saturation. Furthermore, the thesis aims to examine a range of cognitive functions and behaviour, in contrast to previous studies that have often examined only one or two aspects of cognitive functioning, and/or one of two facets of behaviour. To address this, the thesis utilises a wide variety of tests that have been previously used in children. Based on these observations, the overall thesis aims and objectives are:

1. To measure sleep and a range of executive functions in general population sample of UK children aged 6-12 years.
2. To examine whether sleep disturbance (as measured using actigraphy) is associated with deficits in executive function and/or behaviour problems in typically developing children.
3. To examine whether children with cystic fibrosis are at greater risk of sleep disturbance compared to typically developing children.
4. To examine whether sleep disturbance is associated with deficits in executive function in children with cystic fibrosis.
5. To examine whether sleep disturbance is associated with specific deficits in executive function or whether sleep disturbance has an overall negative effect on executive functioning
6. To examine whether sleep disturbance, in the absence of hypoxia, affects executive functioning in a comparable way to sleep disturbance associated with hypoxia.

CHAPTER 5 STUDY 1
SLEEP DISTURBANCE AND NEUROPSYCHOLOGICAL FUNCTIONING IN CHILDREN

5.1. INTRODUCTION

As discussed in Chapter 1, there is a growing body of evidence suggesting that sleep disturbance in children is a risk factor for cognitive and behavioural difficulties. The literature is dominated by studies of sleep-disordered breathing that explain neuropsychological deficits as a consequence of brain abnormalities caused by hypoxia (Beebe & Gozal, 2002). Nonetheless, studies also show such deficits in the absence of SDB, although this research is limited. Some studies have not attempted to accurately assess neuropsychological functioning, instead using school functioning as a measure of cognitive ability. As noted earlier, there is also a lack of consistency in the methods used in different studies to measure cognition. A lack of objective methods of sleep measurement is also absent from the literature, with a reliance on self and parental reports, inevitably due to the time and costs involved in utilising methods such as polysomnography. Steenari et al. (2003) resolved some of these issues in a study of working memory and sleep disturbance in children. They used an objective method of sleep measurement (actigraphy) and a task-specific method of cognitive functioning – an n-back task specifically designed to assess working memory. They found that lower sleep efficiency and longer sleep latency was associated with a higher percentage of incorrect responses in working memory tasks.

The rationale for the present study was to extend the current research evidence, which, as previously noted, is limited. One aim of this study was to replicate the findings of Steenari et al. (2003) in a general population sample of UK children and secondly to extend their study by incorporating additional EF measures. As noted in 2.6.3, there has yet to be a thorough examination of how sleep disturbance affects cognition – with some studies only examining specific cognitive functions. In the study by Steenari et al. (2003), working memory was assessed using the n-back task paradigm. Some authors have argued that it represents a dual-task, involving both a working memory component and a matching subtask (Watter, Geffen, & Geffen, 2001). The n-back task also heavily relies upon attention processes, however Steenari et al. (2003) did not include a pure

attentional measure to distinguish between attention-related and working memory-related aspects of performance deficits associated with sleep quality/quantity. The first study in this thesis aims to examine the relationship between a range of cognitive functions that are considered to be executive functions (based on the theory by Beebe & Gozal presented section 2.7.2) and both subjective parental reports of sleep disturbance as well as objective measures. Previous similar studies have been limited by the use of only subjective or objective reports of child sleep. Furthermore, not all studies using questionnaire methods have used well-validated instruments. In addition this study aims to explore the relationship between sleep disturbance and both cognition and behaviour, in contrast to some studies that have examined either cognition or behaviour independently.

5.2. AIMS

The aims of this study were:

1. To obtain actigraphy sleep data on a general population sample of UK children aged 6 – 11 years.
2. To examine behaviour and a range of executive functions in a general population sample of children aged 6-11 years.
3. To examine the relationship between sleep and executive functioning in a general population sample of children aged 6-11 years.
4. To examine the relationship between sleep and behaviour in a general population sample of children aged 6-11 years
5. To assess the relationship between parental report of sleep and actigraphy measures of sleep in this sample.

5.2.1. Hypothesis

1. Based on the findings of Steenari et al. (2003), it is predicted that higher sleep efficiency as measured using actigraphy, will be associated with better performance on the working memory task of the CANTAB.
2. Based on the findings of Smedje, Broman, & Hetta (2001), parental reports of sleep problems will be associated with increased rates of emotional symptoms, conduct disorder, and hyperactivity.
3. There will be significant correlations between parental report of sleep and actigraphy measures of sleep.

5.3. METHODS

5.3.1. Participants

Primary schools in Andover (Hampshire) and the surrounding villages distributed letters (see Appendix A.1) to parents of children aged 6 – 11 years. Children of primary school age were chosen because of the disruptive effects that adolescence has upon sleep patterns (Carskadon et al., 2004). The letter invited the parent to contact the researcher for further information regarding the study and/or to register their wish to take part. Approximately 14 schools agreed to distribute letters, which totalled around 1500. Of these, 59 parents contacted the researcher. Five families cancelled their appointments leaving the final sample size at 54 (25 girls, 29 boys), *M* = 8yrs 6 months, range 6yrs 0 months - 11yrs 3 months. Due to technical problems, only 43 children had complete actigraph data (19 girls and 24 boys). Technical problems also resulted in missing data for some participant's CANTAB results.

5.3.2. Materials: Sleep

5.3.2.1. Actigraphy

Sleep was measured using wrist-worn actigraphs (Basic Mini Motionlogger, Ambulatory Monitoring Inc., New York), further information and scoring details are given in Appendix G. Actigraphy is activity-based measurement and is considered by some authors (Sadeh, Hauri, Kripke, & Lavie, 1995) as a reliable method for characterising sleep-wake patterns in both disordered and normal sleep. It is recognised by the American Academy of Sleep Medicine (AASM) as a reliable and valid method for detecting normal sleep in healthy population. Actigraphy was chosen as the primary method of sleep measurement to enable a replication/extension of the Steenari et al. (2003) study. Actigraphy provides an objective measurement of sleep periods that is non-invasive and captures information that may not be possible with parent-report alone. For instance, parents may not always be aware of night-wakings in older children, such as the population to be examined in this study. Werner et al. (2008) examined rates of agreement between actigraphy, diary, and questionnaire (constructed by the authors) for the sleep patterns for children aged 4 to 7 years. The differences between actigraphy and diary reports of sleep start, sleep end and assumed sleep were deemed to be satisfactory as the timing differences were less than 30 minutes. However, agreement for actual sleep time and nocturnal wake time were less satisfactory with

differences between diary and actigraphy of ±106 and ±55 minutes respectively. Agreement rates between questionnaire and actigraphy, and diary and actigraphy were deemed insufficient, as all the timing differences were greater than 30 minutes. Polysomnography was not considered a viable option for sleep measurement in this study due to the high cost involved in sleep studies, but also because the intrusive nature of the assessment method risks disruption to the natural sleep pattern of the child and cannot accurately measure social aspects of sleep that may affect children's sleep habits, particularly when they are tested out of the home environment (Stores, Wiggs, & Campling, 1998). Furthermore, PSG is limited by the restricted view that only one or two nights of assessment can provide. Based on previous research (Sadeh, Gruber, & Raviv, 2003) the actigraph variables thought to be of particular interest to this study are:

- Total sleep minutes (actual number of minutes scored as sleep from sleep-onset)
- Sleep latency (minutes taken to fall asleep).
- Sleep efficiency (number of minutes scored as sleep/actual time in bed expressed as a percentage).
- Long wake episodes (number of waking episodes lasting more than 5 minutes).
- Activity Index (the percentage of epochs with >0 activity score, a good indicator of restlessness)

5.3.2.2. Child's Sleep Habits Questionnaire (CSHQ)

While objective measures of sleep are understandably assigned greater credibility in research, parental reports of children's sleep habits provide valuable information not obtainable by PSG or actigraphy. Specifically they can provide information relating to extended periods of time and can explore environmental and behavioural dimensions that influence sleep. The Child's Sleep Habits Questionnaire (CSHQ; Owens et al., 2000b) is a retrospective 45-item parent report sleep-screening instrument designed to assess sleep habits and sleep problems in school-aged children (see Appendix E). The instrument is freely available on the internet[4] and was chosen as there were no validated questionnaires using populations of UK children using this questionnaire (Holley, Hill, & Stevenson, accepted for publication). It is based on common clinical symptom presentations of the most prevalent paediatric diagnoses according to the *International Classification of Sleep Disorders* (American Sleep Disorders Association, 1990). Psychometric properties of the questionnaire have been published and satisfactory test-

[4] www.kidzzzsleep.org/researchinstruments.htm

retest reliability of CSHQ subscales has been reported for both normal and clinical populations (Owens et al., 2000). The total sleep disturbance score consists of 33 items, which can be subdivided into eight subscales: Bedtime Resistance, Sleep Onset Delay, Sleep Duration, Sleep Anxiety, Night Wakings, Parasomnias, Sleep-Disordered Breathing, and Daytime Sleepiness. Items are rated on a three-point scale ranging from (rarely = 0-1 nights per week; sometimes = 2-4 nights per week; usually 5-7 nights per week). Some items are reversed before scoring so that higher scores are uniformly indicative of more disturbed sleep. The CSHQ yields a total sleep score, with higher scores reflecting greater total sleep disturbance. A cut-off total score of 41 has been proposed by the authors of the questionnaire as best able to identify clinical sleep problems. The questionnaire takes approximately 10 minutes to complete.

5.3.3. Materials: Executive Function

5.3.3.1. CANTAB

The Cambridge Neuropsychological Test Automated Battery (CANTAB) is a computer administered cognitive assessment tool designed to assess neuropsychological functioning associated with the frontal lobes such as memory, visual attention, planning, visual memory, and working memory. It was originally developed for use with normal elderly populations and brain-damaged patients. The CANTAB was developed about 15 years ago and has since been used in a number of studies, with standardised and validated normative data available for ages 4 - 90 years of age (Luciana & Nelson, 1998). CANTAB tests have satisfactory levels of test re-test reliability (although retest reliability has not yet been examined in children) and is ideal for use with children for a number of reasons:

- All task stimuli are nonverbal thus reducing any potential performance differences due to language ability
- It can be used with children for whom English is not their first language.
- Children find the computerised testing format to be interesting and motivating (Luciana, 2003).

In addition to these strengths, CANTAB enables a standardised testing procedure that minimises experimenter bias/error. However, the relative expense of the instrument has been documented (Levaux et al., 2007).

Although this study was primarily concerned with measuring working memory and attention, the use of the CANTAB permitted additional subtests to be used with ease and thereby enabling the measurement of additional executive function processes. Thus extending the Steenari et al. (2003) study by measuring a range of executive functions rather than a single process.

Six subtests from the CANTAB were administered using a laptop computer (Tablet PC, Toshiba) and portable touch-screen (Magic Touch, Keytech Inc.). The screen of the laptop could be rotated 180° enabling the keyboard to be hidden from view whilst the child completed the tests. The tests took between 45 minutes and 1 hour to complete depending on the speed of the child.

Intra-Extra Dimensional Set Shift (IED)

This task assesses rule acquisition and attentional set shifting. The child is presented with two patterns and must learn which of the stimuli are correct (and hence the rule) by touching it. After several consecutive correct trials, the rule changes and the child has to learn the new rule. In further trials, the rules continue to change, as do the patterns. Being able to change responses, rather than persevere with the same response, will result in better performance. Two outcomes are reported: the number of errors made in performing the task (IED total errors) and the number of stages completed (IED stage).

Pattern and Spatial Recognition Memory (PRM)

This is a test of visual recognition memory in a 2-choice forced discrimination. Children are presented with 12 patterns, one at a time. In the next phase 2 patterns are presented simultaneously and the child must choose which pattern they have seen before.

Rapid Visual Processing (RVP)

A test of visual sustained attention. Digits from 2 to 9 are presented on the screen, one at a time, in a random order. Children have to identify (by pressing a button) a target sequence of digits (1-2-3). Three outcome measures were analysed: RVP Mean latency, which is a measure of sustained attention. RVP A', which represents how good the child is at detecting target sequences; and RVP B', which represents the tendency to respond, regardless of whether the target sequence is present.

Spatial Working Memory (SWM)

This task assesses visual working memory and strategy use. Coloured boxes appear on the screen and children have to search for hidden tokens. The aim is to find all the tokens whilst remembering not to return to a box where a token was found. Memory load is varied by using 3, 4, 6, and 8 boxes. An efficient search strategy requires the child to remember where they searched previously. The use of the strategy as well as the number of errors made is recorded.

Spatial Memory Span (SSP)

This is a computerised version of the Corsi Blocks task that measures working memory capacity. An array of squares appears on the screen, some of the squares change colour, one by one, in a variable sequence. After a short delay the child must touch the squares in the order that they changed colour. The task begins with only two squares changing colour, but gradually increases, depending on performance, up to nine squares. SSP span is the longest sequence successfully recalled by the child.

Stockings of Cambridge (SOC)

This is a Tower of London task that assesses spatial planning. Two displays representing a stack of coloured balls are presented; the child must move the balls around (by touching them) in the lower display so that it imitates the pattern in the top display. The child is told to try and solve the problem in the minimum number of moves possible (which varies from 2 to 5). For each problem, only a certain number of moves are permitted, so the child is told to think about how they will solve the problem before they begin to move the balls around. The number of problems solved in the minimum moves possible (SOC minimum moves) was the main outcome analysed.

5.3.4. Materials: Behaviour

5.3.4.1. Behaviour Rating Inventory of Executive Function (BRIEF)

To obtain a qualitative insight into children's executive functioning, rather than relying solely on test instruments that may not accurately reflect behavioural manifestations of EF in different situations, an additional parental measure of children's executive functioning was included. The BRIEF (Gioia et al., 2000) is a standardised parent-report instrument that consists of 86 items based on theoretical and empirically based definitions of the EF construct. Normative data have been published for children aged

5-18-years available and the questionnaire takes approximately 10 minutes to complete. Parents rate their child's behaviour on a three-point Likert scale (never, sometimes, and often). Eight scales are obtained (Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor), along with a Metacognition Index (MCI), Behavior Regulation Index (BRI), and a Global Executive Composite (GEC). Higher ratings are indicative of greater perceived impairment. The BRIEF Parent Form was normed on 1419 control children and 852 children from referred clinical groups. Factor analytic studies of the normative sample support the existence of two underlying factors, which have been used to develop the MCI and BRI. Mean internal consistency ratings reported for clinical populations using the BRIEF Parent Form range from .82 to .98. Three-week test–retest correlations for clinical populations on the Parent Form range from .72 to .84. Examples of items from the Working Memory scale include: "forgets what he/she was doing," or "has trouble remembering things, even for a few minutes." Items from the Inhibit scale include: "talks at the wrong times" and "gets out of control more than friends.

5.3.4.2. Strengths and Difficulties Questionnaire (SDQ)

The SDQ (Appendix H) is a brief behavioural screening measure for children aged 3 - 16 year olds that is completed by parents. There are 25-items divided between 5 scales: Emotional Symptoms, Conduct Problems, Hyperactivity, Peer Problems, and a Pro-Social Scale. Psychometric properties of the scale have examined and show the questionnaire to have good reliability and validity (Goodman, 2001). In a study of 132 children aged 4 – 7 years, scores from the SDQ (as completed by mothers) were highly correlated with the Child Behavior Checklist (CBCL). In addition, as judged against a semi-structured interview, the SDQ was significantly better than the CBCL at detecting inattention and hyperactivity, and at least as good at detecting internalizing and externalizing problems. Mothers of low-risk children were twice as likely to prefer the SDQ (Goodman & Scott, 1999). This scale was chosen in preference to others, such as the CBCL, due to its brevity - the questionnaire takes approximately 5 minutes to complete. The brevity of the questionnaire may make the questionnaire more tolerable to parents thereby improving the response rate and accuracy (Widenfelt, Goedhart, Treffers, & Goodman, 2003).

5.3.5. Procedure

Ethical permission was obtained from the School of Psychology, University of Southampton. Information sheets were sent to the parent and child prior to the first visit (se Appendix A.2). The researcher visited the child's home to obtain written consent (see Appendix A.3) and deliver the actigraph and questionnaires. The child was requested to wear the actigraph for at least 72 consecutive hours. They were informed that they were able to remove the actigraph to bath or shower, and also to remove if necessary for school or after-school activities. Parents were asked to complete a sleep diary recording bedtimes, waking times, and estimated time to fall asleep (see Appendix I). This information was used to assist in the analyses of the actigraphy data. The researcher returned to the child's home at the end of actigraphy measurement to carry out the computerised testing. Parents were asked to provide a table and chair in a quiet place for the tests to be administered.

5.3.6. Statistical Analyses

All analyses were performed in SPSS 15.0 for Macintosh (SPSS Inc, Chicago, Illinois). Data distributions were visually checked for normality by plotting histograms and conducting one sample Kolmogorov-Smirnov tests. Table 37 (Appendix A.4) shows the results of the one sample Kolmogorov-Smirnov tests for the sleep variables and the main aggregated dependent variables data (aggregated executive function score, and the total scores from the questionnaires). In order to test for gender effects, either Mann Whitney U or independent t tests were conducted with gender as the IV and sleep, EF, and behaviour outcomes as the DV's. All tests are two-tailed unless otherwise indicated. In order to test the relationship between sleep disturbance and EF and behaviour problems, multivariate analysis of variance (MANOVA) were conducted with high or low sleep disturbance as the independent variable (IV) and the aggregated executive function score and the BRIEF subscales as dependent variables (DV). The total SDQ score was not normally distributed so Mann-Whitney U-tests were used to compare behaviour ratings of high and low sleep disturbance groups. Pearson correlation coefficients were used to assess associations between age and all outcome measures.

5.3.6.1. Adjustment for multiple testing

In this study, and throughout the thesis, statistical significance has not been adjusted to account for the number of tests that have been performed on the study data. The issue of whether or not to adjust for multiple testing is a complex one that has been, and still is

being, widely debated. Perneger (1998) argues that such adjustments are overly conservative and unnecessary unless one is searching for significant associations in the absence of pre-established hypotheses. Nagakawa (2004) argues that presenting effect sizes allows readers to evaluate and make judgements about the importance of results.

5.4. RESULTS

5.4.1. Age and Gender Effects

5.4.1.1. Actigraphy

The actigraphs were worn for an average of 5 days (range 3 – 8 days). As shown in Table 37 (Appendix A4), no significant differences were found between boys and girls on actigraph outcomes (independent samples t test). As would be expected, significant correlations were found among all actigraph variables, however age was not associated with any of the actigraphy outcomes (see Table 42, Appendix A.4).

5.4.1.2. Children's Sleep Habits Questionnaire

Boys and girls did not differ on any subscales or the total score of the CSHQ (Mann Whitney *U* tests, see Table 38, Appendix A.4). Age was not significantly associated with CSHQ subscales or total score (Table 4, page 107).

5.4.1.3. CANTAB

Descriptive statistics (median and interquartile range) for CANTAB measures are shown in Table 39 (Appendix A.4). Boys and girls differed significantly on only one CANTAB outcome, RVP B', girls tended to make fewer false alarms on the RVP test compared to boys ($U = 222.00$, $p < 0.05$). Age was significantly correlated with several CANTAB measures (Table 42, Appendix A.4), so partial correlation coefficients, controlling for age, were also calculated and are shown in Table 2.

5.4.1.4. Strengths & Difficulties Questionnaire (SDQ)

Mann Whitney tests (Table 40, Appendix A.4) were calculated to examine gender differences in SDQ. Consistent with studies of hyperactivity, parents reported more hyperactivity in boys (*Mdn* = 4.50) compared to girls (*Mdn* = 2.00) although this just

failed to reach significance ($U = 236.50$, $p = .07$). Girls were significantly higher on the pro-social subscale compared to boys ($U = 222.00$, $p < .05$).

5.4.1.5. Behavior Rating Inventory of Executive Function (BRIEF)

Age and gender comparisons were not made for BRIEF scores as they are normalised for both age and gender.

5.4.2. Sleep Disturbance and Executive Functioning

The association between sleep efficiency (as measured using actigraphy) and executive functioning was firstly assessed using Pearson correlation coefficients. As shown in Table 42 (Appendix A.4), only one significant correlation was found: better performance on the SOC task was associated with fewer minutes awake after sleep onset (WASO), r (37) = -.31, $p < .05$. After controlling for age (Table 2) neither remained significant although the direction of the effect was still evident. There was a trend for children who performed better on the SOC task to have higher sleep efficiency although this was not significant (r (37) = .273, p = .093).

Sleep quality has yet to be clearly defined in the literature with different researchers using different criteria to establish good and bad sleep quality. For this analysis, an overall sleep disturbance score was derived from three actigraph outcomes proposed to be important for sleep quality: sleep efficiency, sleep latency, and activity index. Children with low sleep disturbance had high sleep efficiency, low sleep latency, and a low activity index. The relationship between sleep quality and cognitive functioning was assessed using a general linear model (GLM) controlling for age and gender. In the model, the overall sleep disturbance score was derived using the sum of standardised scores from the three main actigraphic outcome measures and the median was used to categorise children into two groups, high and low sleep disturbance. Independent samples t test confirmed there was no difference in age between high and low sleep disturbed groups, t (39) = -.43, $p > .05$ or gender, t (39) = -0.62, $p > .05$ (Table 1).

Table 1 Means & *SD* of executive function scores for high and low sleep disturbance

	High sleep disturbance		Low sleep disturbance	
	Mean (SD)	n	Mean (SD)	n
Executive Function	-.465 (1.48)	20	.564 (1.22)	20

Table 2 Partial correlation coefficients between actigraphy and CANTAB controlling for age (n=40)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
SWM total errs	1.00															
SWM strategy	**.61**	1.00														
IED stage	.02	**-.07**	1.00													
IED total errors	.01	.15	**-.86**	1.00												
SOC min moves	**-.38**	-.21	-.12	-.09	1.00											
PRM correct	**-.48**	**-.36**	.09	-.27	.23	1.00										
SSP span	**-.49**	**-.48**	-.08	-.02	.31	.25	1.00									
RVP A	-.17	-.10	.05	-.04	.21	.25	.16	1.00								
RVP B	-.14	-.18	**-.33**	.24	**.39**	-.01	.21	-.13	1.00							
RVP latency	.22	.08	**.34**	**-.46**	.08	.00	-.01	-.05	**-.32**	1.00						
Activity index	-.18	-.11	**.35**	-.16	-.15	.03	-.10	-.02	-.13	-.01	1.00					
LWE	-.05	.02	.19	-.11	-.23	.05	-.01	.02	-.17	.12	**.45**	1.00				
Sleep efficiency	.05	.06	-.12	.05	.27	-.04	.10	.04	.21	-.06	**-.48**	**-.91**	1.00			
WASO	-.10	-.09	.09	-.02	-.25	.06	-.09	-.01	-.21	.06	**.48**	**.90**	**-.99**	1.00		
Total sleep minutes	.05	.15	-.16	.09	.30	-.07	.09	.11	.13	.06	**-.52**	**-.68**	**.84**	**-.81**	1.00	
Sleep latency	.17	.09	.04	.00	-.28	-.25	-.22	-.26	.00	.17	.29	**.45**	**-.52**	**.49**	**-.42**	1.00

Significant correlations, $p < .05$, shown in bold script

(SWM= Spatial Working Memory; IED = Intra/Extra Dimensional Set Shift; SOC = Stockings of Cambridge; PRM = Pattern Recognition Memory; RVP = Rapid Visual Processing; LWE = Long Wake Episodes; WASO = wake after sleep onset)

A total executive function factor score was derived (also using standardised scores) from the sum of three main CANTAB outcome measures: SWM strategy score, SOC problems solved in minimum moves, and RVP mean latency. The executive function factor score served as the dependent variable. As expected, age had a significant effect on executive functioning (F (1, 39) = 6.01, p = .019), but gender did not, (F (1, 39) = 0.002, p = 0.961). Even after controlling for age and gender, the GLM revealed that executive function performance was significantly greater in children with low sleep disturbance compared to children with high sleep disturbance, (F (1, 39) = 5.427, p = .026).

5.4.3. Sleep Disturbance and SDQ

5.4.3.1. Actigraphy and SDQ

Actigraphy sleep variables did not correlate with any SDQ subscales (Table 3). To further explore the relationship between sleep disturbance and parental reports of behaviour using the SDQ, Mann-Whitney U tests were calculated to assess whether children with high sleep disturbance had higher rates of behavioural problems. As shown in Table 41 (Appendix A.4), there were no significant differences between the high and low sleep disturbance groups for any SDQ subscales or the total SDQ score.

5.4.3.2. Parental report (CSHQ) and SDQ

The relationship between parental reports of sleep (CSHQ) and parental reports of behaviour (SDQ) were assessed using Pearson correlation coefficients (Table 4). Age was not included as a covariate as it was not associated with any subscales of the CSHQ or SDQ. Two CSHQ subscales (Parasomnias and Daytime Sleepiness) were significantly associated with nearly all SDQ subscales. Three CSHQ subscales were not associated with any SDQ subscales – Bedtime Resistance, Sleep onset Delay, and Sleep-Disordered Breathing. Likewise, the pro-social SDQ subscale did not show any significant associations with any of the CSHQ subscales. Increased rates of Conduct Problems were associated with higher scores on the CSHQ Sleep Duration (r = .30, p = .03) and CSHQ Sleep Anxiety (r = .30, p = .02). Hyperactivity was significantly correlated with CSHQ Sleep Duration (r = .31, p = .02) and CSHQ Night Wakings (r = .28, p = .04).

Table 3 Correlations between actigraphy and SDQ

	1	2	3	4	5	6	7	8	9	10	11	12
Activity index	1.00											
Long wake episodes	**.51**	1.00										
Sleep efficiency	**-.52**	**-.91**	1.00									
Wake after sleep onset	**.52**	**.91**	**-.99**	1.00								
Total sleep minutes	**-.46**	**-.62**	**.77**	**-.72**	1.00							
Sleep latency	**.30**	**.45**	**-.50**	**.46**	**-.41**	1.00						
Emotional Symptoms	.05	-.07	.06	-.02	-.03	.06	1.00					
Conduct Problems	.08	.06	-.11	.12	-.20	-.04	**.32**	1.00				
Hyperactivity	.27	.22	-.16	.15	-.17	.15	**.47**	**.56**	1.00			
Peer Problems	.23	.12	-.07	.05	-.07	.03	**.66**	**.53**	**.57**	1.00		
Pro-social	-.10	-.11	.02	.01	.01	-.16	-.11	-.21	**-.30**	-.27	1.00	
SDQ	.22	.12	-.09	.10	-.15	.08	**.78**	**.71**	**.85**	**.85**	**-.28**	1.00

Significant correlations, $p < .05$, shown in bold script

Table 4 Correlations between CSHQ and SDQ

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Bedtime Resistance	1.00															
Sleep Onset Delay	**.49**	1.00														
Sleep Duration	**.50**	**.48**	1.00													
Sleep Anxiety	**.60**	**.46**	**.43**	1.00												
Night Wakings	**.42**	**.49**	**.33**	**.57**	1.00											
Parasomnias	**.33**	.16	**.34**	**.30**	**.42**	1.00										
Sleep-Disordered Breathing	.10	.16	.25	.04	.00	.04	1.00									
Daytime Sleepiness	**.33**	**.37**	**.32**	**.34**	.14	.17	-.02	1.00								
Total CSHQ score	**.74**	**.64**	**.73**	**.70**	**.57**	**.59**	.21	**.70**	1.00							
Emotional Symptoms	-.14	.04	.06	.10	**.28**	**.34**	-.01	.19	.19	1.00						
Conduct Problems	.16	.21	**.30**	**.31**	.20	**.42**	.05	**.38**	**.45**	**.32**	1.00					
Hyperactivity	.16	.16	**.31**	.23	**.28**	**.42**	.08	**.32**	**.43**	**.47**	**.56**	1.00				
Peer Problems	-.06	-.02	.11	.02	-.04	**.28**	.13	**.30**	.21	**.70**	**.53**	**.57**	1.00			
Pro-social scale	.11	-.07	-.20	-.12	.12	.17	-.13	-.11	-.04	-.11	-.19	-.30	-.27	1.00		
Total SDQ	.04	.12	.25	.20	.24	**.46**	.08	**.37**	**.40**	**.78**	**.70**	**.85**	**.85**	-.26	1.00	
Age	.17	.08	.12	.00	.00	.17	.12	-.23	.05	-.09	-.14	-.11	-.03	.03	-.11	1.00

Significant correlations, $p < .05$, shown in bold script

5.4.4. Sleep Disturbance and BRIEF

5.4.4.1. Actigraphy and BRIEF

There were no significant correlations between actigraphy sleep variables and BRIEF subscales (Table 45, Appendix A.4). To further explore the relationship between sleep disturbance and parental reports of behaviour using the BRIEF, a multivariate analysis of variance (MANOVA) was calculated with sleep disturbance (as described above) as the independent variable and controlling for age and gender. BRIEF scores of children with high and low sleep disturbance are presented in Table 43 (Appendix A.4). The results of the multivariate analysis were not significant (Table 44, Appendix A.4).

5.4.4.2. CSHQ and BRIEF

Associations between the CSHQ and the BRIEF were explored using Pearson correlation coefficients (Table 46, Appendix A.4). Neither age nor gender were included as covariates as neither showed any association with the CSHQ or BRIEF (which is normalised to take account of age effects). Although the two questionnaires measure different behaviours, they were highly correlated, both in the subscales and overall scores. The association between the total BRIEF score (Global Executive Control) and the total CSHQ score was significant (r (47) = .40, $p > .05$).

5.4.5. Parental Report of Sleep and Actigraphy

The correlations between CSHQ subscales, actigraphy variables, and age are shown in Table 5. Parental reports of child sleep correlated well with objective actigraph data. Greater bedtime resistance was associated with lower sleep efficiency, (r (40) = -.336, $p < .05$) and more long wake episodes (r (40) = .33, $p < .05$). Longer sleep latency (actigraphy) was associated with less sleep duration (as reported by parents) (r (40) = .391, $p < .01$), and increased Sleep Anxiety (r (40) = .342, $p < .05$). Parental reports of Night Wakings were significantly associated with lower sleep duration (r (40)= -.392, $p < .01$) and longer sleep latency (r (40) = .326, $p < .05$). The total CSHQ score was significantly associated with actigraphy sleep latency (r (40) = .341, $p < .05$); total sleep minutes (r (40) = -.31, $p < .05$); and sleep efficiency (r (40) = .314, $p < .05$). Actigraphic sleep measures were not associated with parental reports of sleep-disordered breathing or daytime sleepiness.

Table 5 Correlations between actigraphy, CSHQ, and age

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Activity index	1.00															
Long wake episodes	**.49**	1.00														
Sleep efficiency	**-.51**	**-.92**	1.00													
Wake after sleep onset	**.52**	**.91**	**-.99**	1.00												
Total sleep minutes	**.46**	**-.62**	**.78**	**-.73**	1.00											
Sleep latency	.28	**.45**	**-.52**	**.48**	**-.41**	1.00										
Bedtime resistance	.07	**.33**	**-.34**	.26	**-.35**	.26	1.00									
Sleep-onset delay	-.15	-.07	.07	-.05	-.13	.27	**.47**	1.00								
Sleep Duration	.13	**.30**	-.29	.21	-.28	**.39**	**.42**	**.38**	1.00							
Sleep Anxiety	.04	.05	-.10	-.09	-.14	**.34**	.16	.22	.14	1.00						
Night Wakings	.27	.09	-.24	.23	**-.39**	**.33**	.14	**.40**	.21	**.38**	1.00					
Parasomnias	.18	.17	-.28	**.28**	**-.47**	-.09	.08	.08	.26	-.02	.36	1.00				
Sleep-Disordered Breathing	-.25	.02	.01	-.03	.20	.10	.00	.20	.28	-.04	-.07	.00	1.00			
Daytime Sleepiness	-.06	.03	.00	.00	.05	.10	.18	.27	.11	-.05	-.10	-.07	-.01	1.00		
Total CSHQ score	.00	.24	**-.31**	.25	**-.38**	**-.34**	**.57**	**.65**	**.69**	.28	**.43**	**.48**	.24	**.53**	1.00	
Age	-.27	-.26	-.21	.27	-.10	-.02	.15	.14	.23	.07	-.04	.24	.08	-.18	.13	1.00

Significant correlations ($p < .05$) in bold script

5.4.6. Validity of Executive Functioning Measures

The CANTAB is a computerised testing battery that is designed to assess various domains of executive functioning. Likewise, the BRIEF is a parental questionnaire designed to assess behavioural manifestations of EF. The two measures should be highly correlated if they are both assessing the same construct. Pearson correlation coefficients were used to assess whether significant associations exist between the two measures (shown in Table 47, Appendix A.4). The CANTAB SWM test measures working memory and both the strategy score (r (49) = .33, p < .05) and the total errors score (r (49) = .35, p < .05) were significantly associated with parental reports of working memory from the BRIEF. The BRIEF measure of working memory was also significantly correlated with the CANTAB test of Spatial Span (r (49) = .43, p < .05). The CANTAB SOC (Stockings of Cambridge) test is a measure of planning and was significantly correlated with the Plan/Organize subscale of the BRIEF (r (49) = .36, p <.05). Hence, although several significant associations were demonstrated between the CANTAB and the BRIEF, the two measures do not correlate as well as might be expected.

5.5. DISCUSSION

5.5.1. Aims of the Study

1. To obtain actigraphy sleep data on a general population sample of UK children aged 6 – 11 years.

Actigraphy data were successfully collected for 43 children, and was demonstrated to be a simple yet objective method of sleep measurement in children. The results of the sleep data are comparable to that found in the Finnish study by Steenari et al. (2003) who report a mean sleep efficiency of 86.50, similar to the average sleep efficiency score obtained in this study. They also reported a significant difference in sleep efficiency between boys and girls, although no such difference was found in this study.

2. To examine behaviour and a range of executive functions in a general population sample of children aged 6-11 years.

A range of executive functions were measured using the CANTAB and behaviour was measured using the SDQ and the BRIEF.

3. To examine the relationship between sleep and executive functioning in a general population sample of children aged 6-11 years.

A third aim of the thesis was to investigate possible associations between sleep disturbance (as measured using actigraphy and parent report) and cognition and behaviour, these findings are summarised below.

5.5.2. Relationship between Actigraphy and CANTAB

The main hypothesis of this study was based on the findings of Steenari et al. (2003) who found that better working memory performance was significantly correlated with higher sleep efficiency, longer sleep duration, and lower sleep latency. However, similar associations were not found in this study and the hypothesis that better sleep efficiency would be associated with better working memory was not supported. Better performance on the planning task was significantly associated with lower night-time activity although after controlling for age this was no longer significant (p = .052). No other significant correlations between sleep efficiency and other EF measures, or other actigraphy sleep variables and EF measures were found.

The lack of specific correlations in this study is also in contrast to Sadeh, Gruber, and Raviv (2002) who like Steenari et al. (2003) demonstrated significant correlations between actigraphy measures and neuropsychological tasks. However, the results of Sadeh et al. (2002) did not demonstrate a clear pattern of associations between neuropsychological measures and actigraphy sleep measures, nor are they wholly consistent with the findings of Steenari et al. (2003). For example, sustained attention was correlated with Night Wakings but not with sleep duration. Furthermore, as noted earlier, spatial working memory did not correlate with any sleep measures. These inconsistent results may be, at least in part, attributable to the lack of standard criteria for defining sleep quality, which is discussed in the section on methodological limitations.

The GLM analysis pooled performance on three EF tasks as an overall measure of executive functioning and also calculated an overall sleep quality score on the assumption that sleep disturbance may be a consequence of several related factors. The three sleep variables selected to represent sleep disturbance in this study were: Sleep efficiency, a measure (expressed as a percentage) of how much time is actually spent asleep whilst in bed; sleep latency, which is a measure of how long it takes to fall asleep, and the activity index, which is a measure of the amount of activity during the night.

As described in the results section, these three variables were summed (using z scores) to produce an overall sleep disturbance score, which was split at the median to produce a high sleep disturbance group and a low sleep disturbance group. However, this analysis was not an a priori hypothesis but was conducted post-hoc. Furthermore, it could be argued that the criteria used in this study for defining "poor sleep" lacks clear empirical basis as no previous studies have pooled three actigraph measures. Nonetheless two of the three sleep measures used (sleep latency and sleep efficiency) were both associated with neuropsychological functioning in previous studies (Steenari et al., 2003; Sadeh et al., 2002). The third measure, activity level, was included as it was proposed that increased night-time activity may represent increased sleep disturbance. The results of this analysis did suggest that executive functioning was improved in children with higher sleep quality. It may therefore be that sleep quality is better

represented by a combination of sleep measures, rather than simply defining good sleep quality on the basis of a single outcome.

5.5.3. Thesis Aim 4: To Assess the Relationship Between Sleep and Behaviour

Another aim of this study was to examine the relationship between sleep and behaviour in a general population sample of children aged 6-11 years. In this study, sleep quality as defined for the GLM analysis was used to explore differences in children's behaviour as characterised by the SDQ using Mann-Whitney U-tests. Sleep quality measured using actigraphy was not related to parental reports of behaviour. Previous studies have also failed to establish an association between parental reports of behaviour and actigraphy (Aronen, Paavonen, Fjallberg, Soininen, & Torronen, 2000), although they did find a relationship between teacher reports of externalising behaviour problems and sleep time.

Hypothesis 2

Although actigraphy sleep measures did not correlate with behaviour reports, parental reports of sleep were significantly associated with the SDQ. Correlations between the two questionnaires were most notable for parental reports of Parasomnias, which was associated with increased rates of Emotional Symptoms, Conduct Problems, Hyperactivity, and Peer Problems. Elevated reports of Daytime Sleepiness were associated with higher scores on Conduct Problems, Hyperactivity, and Peer Problems. These findings are consistent with previous research: higher rates of behaviour problems in children (as measured using the SDQ) have previously been associated with parental reports of sleep disturbance (Smedje, Broman, & Hetta, 2001). Furthermore, ADHD symptoms have also been associated with parental reports of sleep problems (Chervin et al., 2002).

Similar results were obtained for the BRIEF questionnaire. None of the BRIEF subscales were associated with any actigraphy sleep measures. The MANOVA failed to find an effect of sleep disturbance as measured using actigraphy on BRIEF subscales. However, parental reports of sleep did correlate with BRIEF subscales. Of note are the significant correlations between the overall BRIEF score (global executive control; GEC) and parental reports of Sleep Anxiety, Parasomnias, and Daytime Sleepiness. Overall, higher sleep disturbance (total CSHQ score) was associated with increased reports of behaviour manifestations of EF problems.

5.5.4. Thesis Aim 5: Parental And Objective Reports of Sleep

A final aim of this thesis was to examine the relationship between parental report of sleep and actigraphy measures of sleep.

Hypothesis 3

A third hypothesis of this study – there will be significant correlations between parental report of sleep and actigraphy measures of sleep – was supported. A positive relationship was demonstrated between the actigraphy sleep measures and parental reports of sleep using the CSHQ. The strongest association was found between parental reports of Night Wakings and the activity level recorded by the actigraphy. These results are in contrast to previous research, which has found inconsistencies between parental reports of sleep and actigraphy sleep measures, at least for parents of children with ADHD (Wiggs et al., 2005). Present findings suggest that the CSHQ is a useful tool for the assessment of sleep disturbance in healthy, typically developing children.

5.5.5. Methodological Limitations

5.5.5.1. Sample limitations

The study sample size was relatively small (total n = 55, but only 44 had actigraphy data), particularly in terms of statistical power assumptions. According to Cohen (1992) to find a medium effect size (r = .30) with power at .80, and probability at .05, requires 85 participants. Steenari et al. (2003) had a greater number of children (n = 66), which may partly explain the discrepancies between the two studies. Several factors contributed to a smaller sample size than originally intended. Firstly, several appointments were made and then cancelled some as a result of family crisis and other parents gave no reason for the cancellation. Actigraphy data were lost for some participants due to technical difficulties with the actiwatch that either prevented the data from being recorded or from being accurately retrieved. The CANTAB also failed on several occasions, when the computer shut down the program midway through the battery of tests.

During the cognitive testing, it was also noted that some children exhibited significant behaviour difficulties, which appeared to affect their ability to perform the task, although no formal diagnoses were disclosed to the researcher. For example one male child was unable to concentrate for any length of time on the tasks and had to be repeatedly reminded to attend to the computer. Thus the sample may not have been

representative of the general population, but rather was over-represented by children with behaviour problems, unlike the sample in the Steenari et al. (2003) study. Children with behaviour problems may have had difficulty with the tasks and performed badly compared to other children but they may have had normal sleep patterns.

5.5.5.2. Measurement limitations

The CANTAB was designed for use with an elderly population and to measure EF in brain-damaged populations. Although the CANTAB has been used with children, during this study children often appeared impatient to complete the tasks and/or did not appear to totally understand what was required of them on several tasks. Furthermore, although the CANTAB has been validated for use with children from age four, as with all tasks that purport to measure EF, there are limitations as to the information that can be extracted. Most, if not all, executive tasks will activate non-executive processes that may be unrelated to the task, or may in fact be necessary for accurate performance; therefore any task performance measure will also reflect the performance of non-executive processes. This task impurity is argued to be a high degree of measurement error in executive tasks (Burgess, 1997). The complexity of EF tasks is also an issue when attempting to differentiate the performance of distinct executive processes. Many EF tasks require the execution of several processes thought to underlie executive functioning, consequently task scores will be a product of various executive processes pooled together (Hughes & Graham, 2002). For example the SWM task requires one to be sufficiently attentive as well as involving an element of planning.

Although there were limitations in measuring specific executive functions, the GLM analysis, has to a certain extent, overcome some of these issues by pooling performance on three of the EF tasks so that the aggregated EF score attempts to capture the common variance across these three EF measures, rather than attempting to be process-specific. There was no strong theoretical reason for deciding which of the CANTAB subtests to include in the aggregate score, nor for expecting performance on any particular subtests to be more affected by sleep disturbance. CANTAB provides a number of different data outcomes for each of the different subtests and no published papers were found that suggested which of the variables best represented the underlying EF ability. Hence for working memory, the SWM strategy score was chosen as it represents the efficiency with which participants conduct their searches over the whole task. This was deemed preferable to one of the several outcomes that measured error rates from the different

memory levels. For a measure of sustained attention, the RVP latency measure was chosen and for a measure of planning the Stockings of Cambridge problems solved in minimum moves was chosen as it also represents an overall performance for the task.

5.5.5.3. Defining sleep quality

The inconsistent results obtained by studies examining sleep and executive functioning highlight the difficulties in how best to define sleep quality in children using actigraphy. There is a lack of standard criteria for defining poor sleep quality from actigraphy data in children; in truth, researchers decide which variables to utilise to define sleep quality. There are also issues concerning the distinction between poor and normal sleep (Sadeh, Gruber, & Raviv, 2002). Actigraphy produces numerous variables, any of which could be used to define sleep disturbance. Indeed, previous studies have frequently used different actigraphy outcomes as a measure of sleep disturbance. Steenari et al. (2003) used sleep efficiency, sleep duration, and sleep latency as the variables of interest, whereas Sadeh et al. (2000) defined poor sleepers as children whose sleep efficiency was less than 90% *and* who awoke more than three times per night (with each waking episode lasting more than 5 minutes). Further research is required to establish which actigraphy measures are fundamental in defining sleep quality. For instance, is sleep duration more important than night wakings? Is sleep time a better predictor of sleep disturbance than sleep efficiency? It is probable that several sleep measures are needed to characterise sleep quality, indeed this was the theoretical basis for the GLM analysis that was carried out.

Although actigraphy defines sleep quality using physiological variables based on activity measurement, it provides no information on sleep staging, unlike polysomnography. Polysomnography studies use the information from EEG sleep architecture regarding sleep stages, as well as other variables such as eye movements and chest movements. Understanding the factors that are important to a good night's sleep and subsequent executive functioning may require the additional information that is obtained in PSG studies. However, the issues surrounding the conceptualisation of sleep quality in children are not restricted to actigraphy methodology, there is also no standard criterion for defining sleep quality in PSG studies.

These issues generate many questions regarding the nature of sleep quality that have yet to be answered. What is sleep quality? How can it be accurately defined? Should we use

physiological indicators such as those used in actigraphy and polysomnography? Are subjective variables better indicators of how well someone sleeps? Does sleep quality affect a third unknown variable (such as mental health) that in turn affects executive functioning? Further research is required to answer these questions.

5.6. CONCLUSIONS

The study failed to replicate the results of Steenari et al. (2003) demonstrating that higher sleep efficiency is related to better working memory performance. Post-hoc analysis suggests that sleep quality may be better defined using a combination of sleep measures rather than a single sleep measure. Increased sleep disturbance, as defined using an aggregate measure of three sleep variables had a detrimental effect on children's overall executive functioning, but not on individual tasks.

CHAPTER 6 STUDY 2
SLEEP DISTURBANCE AND NEUROPSYCHOLOGICAL FUNCTIONING IN CHILDREN II

6.1. INTRODUCTION

Chapter 5 examined sleep disturbance and neuropsychological functioning in a sample of children aged 6-11 years. In contrast to previous research demonstrating associations between individual actigraphy measures and measures of EF (Steenari et al, 2003; Sadeh et al., 2002), Study 1 failed to demonstrate simple relationships between sleep disturbance and neurocognitive functioning. However, Study 1 did show that when the sleep variables were aggregated (combining activity level, sleep efficiency, and sleep latency into a global sleep indicator) poorer sleep (lower sleep efficiency, longer sleep latency, and increased activity) was associated with reduced EF (from aggregated measures). As discussed in Chapter 5, several methodological issues arose concerning the use of the CANTAB in measuring EF in children. Although the CANTAB has been used with children, during Study 1 some children often appeared impatient to complete the tasks and/or did not appear to wholly understand the task procedures. Study 2 attempts to resolve these issues by exploring alternative methods to assess EF in children. Furthermore, greater emphasis is placed on the model of prefrontal dysfunction proposed by Beebe & Gozal (2002), as a theoretical basis for determining which executive functions should be examined. With regards to the sleep variables to be explored, Study 1 included activity level in the aggregate measure of sleep disturbance, however, further examination of the sleep literature showed that this measure is not routinely used when examining actigraphic sleep outcomes in children. Hence a decision was made to remove this variable from the aggregate measure.

As described in Chapter 2, section 2.7.2.1, Beebe & Gozal's (2002) model highlights six areas of EF that are proposed to be affected by sleep disturbance. These are behavioural inhibition, set-shifting, self-regulation of affect and arousal, working memory, analysis/synthesis, and contextual memory. Although the model was developed to account for executive dysfunction caused by obstructive sleep apnoea, it could also be used to explain deficits in EF caused by sleep disturbance with no associated sleep-disordered breathing. Sleep disturbance and hypoxia are conceived as two independent factors in the model, and Beebe & Gozal (2002) do not specify the

exact input of these two factors upon the prefrontal cortex and its subsequent functioning. Furthermore, Horne (1988) has argued that the PFC is particularly sensitive to the effects of sleep disturbance.

6.1.1. Rationale for Study 2

Study 2 was designed to extend and enhance Study 1. Although Study 2 is replicating the investigation of sleep disturbance and neuropsychological performance in typically developing children, there are several key enhancements. Firstly, Study 1 did not include an objective measure of SDB. Given the evidence presented in section 2.7 regarding the relationship between SDB and deficits in cognition and behaviour, it is important to exclude the possibility that any associations found between sleep and cognition or behaviour are not a consequence of SDB problems. To resolve this issue, Study 2 will include pulse oximetry to measure overnight oxygen saturation. Furthermore, Study 2 attempts to better reflect the model of sleep disturbance and executive function proposed by Beebe & Gozal (2002) by attempting to incorporate the cognitive functions they clearly specify in their model. Thirdly, Study 2 includes a measure of processing speed. Recent research has demonstrated that processing speed performance is comprised in children with SDB (Hill et al., 2006). In children aged 3-7 years, the WISC processing speed index was significantly lower in children with mild SDB compared to controls. Blunden et al. (2000) also measured processing speed in children with SDB using the WISC, however they only report the individual subtests scores that are used in the WISC processing speed quotient rather than the overall score. The data they report suggests that control children perform better than children with SDB on the processing speed subtests. The literature presented in 2.7 shows similarities in the neuropsychological deficits associated with general sleep disturbance and SDB. Hence it is plausible that if deficits in processing speed are associated with SDB, that deficit may also be evident in children with sleep disturbance but no known medical condition. These issues raise several important questions about the relative importance of SDB as a pathophysiological mechanism for neuropsychological deficits, which are addressed in this section.

A fundamental question that has not been adequately addressed in the literature concerns whether the neuropsychological and behavioural deficits associated with sleep disturbance and sleep-related breathing problems are caused by different or identical pathways.

Although the data presented in Study 2 is of a sample of typically developing children, at the outset the intention of Study 2 was to explore the relationship between sleep and executive function in children with asthma and eczema. Previous studies have found that children with asthma and children with eczema have greater sleep disturbance. Research has also been conducted investigating whether children with asthma perform less well than healthy children on various cognitive tasks, however this evidence is inconclusive. No previous studies have examined the cognitive abilities of children with atopic dermatitis and whether this differs from healthy children without eczema. This is an important area to research as many children have both asthma and atopic eczema, which may place them at even greater risk for sleep disturbance. This may in turn lead to increased cognitive and behavioural difficulties, which may have an effect on school functioning and academic performance. If children with asthma and eczema were identified as experiencing greater sleep disturbance due to night−time symptoms of their illness, the importance of treating night−time symptoms would be highlighted to health professionals. Hence the original plan for Study 2 was to examine neuropsychological performance in four-group design. This was to comprise a sample of children who were at risk of SDB problems (children with asthma), a sample of children at risk of sleep disturbance (children with eczema), a sample of children with co-morbid asthma and eczema, and a group of healthy controls. This design was an attempt at better characterising the nature of the relationship between sleep disturbance and EF. However, due to recruiting issues it was not possible to complete this study and the subsequent clinical group examined in Study 3 comprises children with CF (see Chapter 7).

6.2. AIMS OF STUDY 2

1. To examine the specific effects of sleep disturbance on executive function.

As noted in Chapter 4, one aim of this thesis is to determine whether sleep disturbance is associated with specific deficits in executive function or whether sleep disturbance has an overall negative effect on executive functioning. Study 2 will examine this research question by using the model proposed by Beebe & Gozal (2002). Their model clearly specifies a range of executive functions thought to be affected by sleep disturbance associated with obstructive sleep apnoea. However, as noted above, the model could be used to explain deficits in EF caused by sleep disturbance with no

associated sleep-disordered breathing. This study will examine five of the six executive functions described by Beebe & Gozal (2002). The sixth, contextual memory, has not been included because, as Beebe & Gozal (2002) themselves admit, it is not an executive function. They include it in their original model due to evidence showing that temporal memory is adversely affected by sleep deprivation (Harrison & Horne, 2000). This thesis aims to examine the effects of sleep disturbance on EF rather than on learning and memory, which is a separate, albeit related, issue. Furthermore, Beebe & Gozal (2002) do not specify the effects of sleep disturbance on attention. The performance of any task will be affected by a child's attentional capacity; hence measures of attention have also been included. To ensure that any differences in EF can be attributed to differences in sleep quality and quantity, rather than general deficits in cognition, additional non-executive measures of cognition were included

2. To compare the relative importance of sleep quality versus sleep quantity.
As highlighted in Chapter 5, the literature has yet to clearly identify which measures of actigraphy best represent sleep disturbance. Study 1 used activity level, sleep efficiency, and sleep latency. Study 2 aims to examine in more detail the relative importance of sleep quality and sleep quantity upon children's executive functioning. Sleep quality will be characterised using sleep efficiency (since this indicates the percentage of time actually spent asleep from sleep-onset to sleep-offset). Sleep quantity will be assessed using total sleep minutes (actual minutes scored as sleep from sleep-onset to sleep-offset). Sleep duration (total time from sleep-onset to sleep offset) was not used as an indicator of sleep quantity, as this measure does not account for any periods of waking during the night.

3. To explore the relationship between sleep disturbance and processing speed.
In addition, Study 2 aims to investigate the impact of sleep disturbance on processing speed. Previous research has demonstrated significantly lower processing speed in children with mild sleep-disordered breathing (Hill et al., 2006). To the best of my knowledge the relationship between processing speed and sleep disturbance has not been examined in children with no SDB problems.

4. To examine associations between sleep disturbance and parental report of behaviour.
Although Study 1 did not find any significant associations between sleep disturbance and behaviour problems, this will be further explored in Study 2.

5. To obtain pulse oximetry data on this sample of non-referred children.

6.3. HYPOTHESES

1. Children with higher sleep disturbance (the independent variable, defined as shorter sleep time and lower sleep efficiency), in the absence of sleep-disordered breathing, will have poorer overall executive functioning (dependent variable) compared to children with low sleep disturbance.
2. Non-executive measures of cognition (digit recall) will not be associated with sleep disturbance (defined as shorter sleep time and lower sleep efficiency).
3. Children with high sleep disturbance (the independent variable, defined as shorter sleep time and lower sleep efficiency) will have lower processing speed (the dependent variable) compared to children with low sleep disturbance.
4. Parental reports of behaviour problems (as measured using the SDQ) will be associated with sleep problems (as measured using actigraphy and parental report). In particular, children with high sleep disturbance (the independent variable) will have higher rates of conduct problems (dependent variable).

6.4. METHOD

6.4.1. Participants

Children aged 6 – 12 years were recruited from local schools. Letters were sent out to parents (Appendix B.1) with a brief description of the study and a reply slip with freepost envelope was provided. Approximately 800 letters were distributed via 5 schools, and 75 parents responded, giving a response rate of 8%. From the 72 responses, four parents were unable to be contacted using the details supplied. The remaining 68 parents were contacted by telephone and the study was described to them in more detail. Children were excluded if they had a history of ADHD, learning difficulties defined as a statement of special educational needs, a history of head injury or any other serious psychological or medical condition. Three children were excluded because the parents reported they had a history of ADHD and two parents decided not to participate. Three parents cancelled their first appointment because the child no longer wished to participate, and one child did not complete the study. The remaining sample consisted of 59 children – 27 boys and 32 girls aged 6 years 2 months to 12 years (mean age 9

years 3 months). Boys and girls did not differ with regards to age (t (1,57) = 0.836, df = 57, p = .407). The majority of children lived in a two-parent household (47), 3 children lived with a single parent, and 3 children had parents who were separated or divorced. Table 6 shows the educational background statistics of the parents of the sample.

Table 6 Educational achievements of participant parents

	Mothers	Fathers
No qualifications	7 (12%)	10 (7%)
GCSE/O Levels	20 (34%)	22 (37%)
A levels/NVQ/Highers	23 (39%)	15 (25%)
Degree	5 (9%)	3 (5%)
Postgraduate degree	3 (5%)	3 (5%)

6.4.2. Measures: Sleep

6.4.2.1. Actigraphy

Actigraphy is described in detail in Chapter 5, section 5.3.2.1. Children were instructed to wear the actigraphs continuously for seven days and nights (mean number of nightly recordings = 6, range = 3 – 9 nights). Data were averaged across the number of nights. The two main variables of interest in Study 2 are: total sleep minutes (number of minutes scored as sleep from sleep-onset to sleep-offset); and sleep efficiency (the percentage of time scored as sleep from the first sleep-onset period to the last sleep-offset period).

6.4.2.2. Pulse oximetry

To exclude the possibility that any deficits in EF were the result of sleep-disordered breathing problems, overnight home pulse oximetry was undertaken for one or two nights. Overnight oxygen saturation (SpO_2) was studied using a Masimo Radical pulse oximeter (Masimo- Artemis, UK) sampled at 1HZ and using a 2-second averaging time. Masimo's are small handheld devices, often used in a clinical setting (see Appendix F for image and instructions given to parents). Parents were instructed to attach the SpO_2 probe to the child's middle or index finger when the child was settling to sleep and to remove it when the child awoke in the morning. Studies were performed at home in the

child's familiar sleeping environment. Data analyses were performed with Download 2001 software (Stowood Scientific – Oxford UK). Poor perfusion, low signal IQ and movement artifact data were rejected. Any reports where artifact free data of less than 5 hours duration were collected were rejected. This approach increased the likelihood that representative sleep cycles were sampled, in particular REM sleep episodes where obstructive events are most likely to occur, and is consistent with previously reported methods (Urschitz et al., 2003). Analysis software yields a number of measures but those of interest to this study are: mean SpO_2 (SAT), minimum SpO_2 (SpO_2 nadir), number of desaturations > 4% per hour, and delta 12s index (a measure of the variability in SAT). The latter is calculated as the absolute differences between successive 12 second intervals (sum of the absolute difference divided by the number of intervals measured).

There is a lack of universally agreed oximetry reference values to determine a likely diagnosis of SDB in children. In adult populations delta indices of 0.4 and 0.63 and above, were found to predict an apnoea/hypopnoea index of $\geq$15 with sensitivities of 88% and 91% respectively. In children, however, lower apnoea/hypopnoea indices of $\geq$5 are generally accepted as a threshold to define clinically significant sleep disordered breathing and the predictive value of the delta index has not been published in child populations. A community study (using Masimo technology) of 58 primary school children with no respiratory complaints reported the SpO_2 nadir mean = 93.1 (*SD* = 2.2), range 85-97% and desaturations > 4% /hour of mean 0.9 (*SD* = 0.8), range 0 – 4.4 (Urschitz et al., 2003b). Baseline values of SpO_2 < 97% were uncommon although means and ranges were not provided for this parameter. Urschitz et al. (2003) suggest that the nadir SpO_2 is an accurate predictor of neurocognitive impairment in children and may be used as a standard variable in the evaluation of children. Their study defined mild hypoxemia as nadir SpO_2 = 91%-93%.

For the purposes of this study, each child's oximetry reports were examined to determine the likelihood of sleep-disordered breathing. Previously published data were used to obtain oximetry reference values. A lower threshold of > 2 standard deviations below the lowest mean published data for SpO_2 baseline and nadir values were selected for this parameter (Traeger et al., 2005). Combining these data, the threshold for determination of SDB was: two or more abnormal parameters = probable SDB diagnosis; one abnormal parameter (with the exception of abnormal nadir alone) =

possible SDB diagnosis. The threshold oximetry values used to determine probable sleep disordered breathing were: baseline SpO_2 < 95%; SpO_2 nadir < 86%; delta 12s index > 0.4; desaturation 4% index > 4.

6.4.2.3. Children's Sleep Habits Questionnaire

As described in Chapter 5 (section 5.3.2.2), the Child's Sleep Habits Questionnaire (CSHQ) is a validated sleep-screening instrument designed to assess a variety of sleep behaviours and sleep habits in children.

6.4.3. Materials: Executive Function

As noted in Chapter 5 and discussed in the rationale for this study, rather than use the CANTAB, a different set of executive function tests were chosen for Study 2. Although CANTAB has an easy-to-use computerized format with minimal opportunity for user error, it was noted that not all children appeared to complete the tasks as required. For Study 2, tests were chosen that had a theoretical link to the model of sleep and prefrontal cortex dysfunction proposed by Beebe & Gozal (2002) as detailed in 2.7.2.1. Hence it was important to choose a battery of tests that would include measures behavioural inhibition, self-regulation of affect and arousal, working memory, set shifting, and analysis/synthesis (but not contextual memory as Beebe & Gozal themselves admit it is not really an executive function). Measures of attention were also important to explore, as noted in Chapter 5, the effect of sleep disturbance on attentional processes. The Test of Everyday Attention for Children (TEA-Ch) was chosen as it was the only standardized assessment that could be found that is designed to comprehensively measure (in children) different facets of attention (i.e. divided attention, sustained attention, and selective attention). To measure working memory, the Automated Working Memory Assessment (AWMA) was chosen because of its computerised format (that children seem to enjoy), it was recommended by other post-graduate colleagues as acceptable by children in this age range, and it has satisfactory validity (Alloway, Gathercole, Kirkwood, & Elliott, 2008). Prior to choosing the AWMA, a computerised n-back task, similar to that used by Steenari et al. (2003), was designed and piloted on a few children. However, children seemed unable to fully complete (and understand) the task, hence alternative assessments of working memory were explored. The WISC processing speed measure was chosen as it was the only standardized measure that could be found designed to measure processing speed in

children. Finally, the NEPSY Tower and verbal fluency tasks were chosen to measure planning and verbal fluency. The method of measuring verbal fluency by asking participants to generate as many words as possible beginning with a specified letter (or in semantic form by generating words that belong to a category e.g. animals) is extensively used in executive function research (Phillips, 1997). The Tower of London task is widely used in child populations to measure planning, the NEPSY version was chosen because it has been specifically designed for use with children. Furthermore, additional tests were included that were not thought to measure EF to test for the specificity of the association between sleep disturbance and executive function.

6.4.3.1. Test of Everyday Attention for Children (TEA-Ch)

The TEA-Ch is a standardised and normed clinical assessment battery developed to measure across different attentional capacities of children aged from 6 to 16 years. It was designed to minimise demands on other abilities, such as motor speed and memory. The use of language in both the task stimuli and instructions is limited.

Sky Search

A non-linguistic visual search task of selective attention. The child is presented with a laminated A3 sheet depicting rows of paired spacecraft. Four distinctive types of craft are presented, with most pairs being of mixed type. Children are instructed to try and find all of the target items, defined by a pair of identical craft, as quickly as possible. Twenty targets are distributed among 108 distractors. Termination of the task is self-determined with the child marking a box in the lower left-hand corner to indicate they had finished. In order to control for differences that are attributable to motor speed, rather than visual selection, children complete a motor control version of the task. The A3 sheet is identical to that of the Sky Search test with the exception that all of the distractor items are removed. The task consists of circling all twenty target items as quickly as possible and then indicating completion as before. Outcomes from the task are time taken to completion, accuracy (number of spacecraft pairs correctly identified), and a time-per-target score.

Score

The Score subtest is a 10-item tone-counting measure of sustained auditory attention. In each item, between 9 and 15 identical tones of 345ms are presented, separated by silent interstimulus intervals of variable duration (between 500 and 5000 ms). Children are

asked to silently count the tones (without assistance from the fingers) and to give the total at the end. Child must keep count of a series of sounds presented in an irregular manner.

Creature Counting

A visual task of attentional control, which requires the child to switch from one mental set to another. The stimulus consists of a page (7 items) with a variable number of "creatures" depicted in their burrow. Interspersed between the creatures were arrows either pointing up or down. The children are asked to count the creatures from the top down but to use the arrows as a cue to switch the direction of their count. Accuracy of response and the time taken to complete each item is recorded. The task is analogous to Beebe & Gozal's (2002) concept of set-shifting.

Sky Search DT

A dual task measure of divided attention. Children are asked to complete a parallel version of the Sky Search task, which differed only in the location of the targets. As they perform the visual search, they are asked to simultaneously and silently count the number of tones presented within each item of an auditory counting task. Although the counting task used the same stimuli as the Score subtest, a regular pacing of one tone per second is used. A higher score indicates poorer performance.

Score DT

A test of auditory sustained and divided attention designed to increase the sensitivity of the basic score task by including a distractor. The tone-counting aspect of the task is identical to that of score described above. In addition, meaningful, auditory speech – in the form of news bulletins – are presented simultaneously. During each of 10 news reports, the child must recall the number of tone-counts and the name of animal mentioned in the news bulletin.

Opposite Worlds

A task of attentional control and also measures verbal behavioural inhibition. Children are presented with a stimulus sheet showing a mixed, quasi-random array of the digits 1 and 2. In the 'Same Worlds' condition they are asked to read out the digits aloud as quickly as possible. The purpose of the 'Same Worlds' condition is to reinforce the prepotent response to name the numbers in the conventional manner in the context of

the test materials. In the 'Opposite Worlds' condition children are asked to say the opposite for each digit – "one" for 2 and "two" for 1 – as quickly as possible, inhibiting the prepotent verbal response. The time taken to complete each item is recorded.

6.4.3.2. NEPSY

The NEPSY: A Developmental Neuropsychological Assessment (NEPSY; Korkman, Kirk, & Kemp, 1998) is a standardised measure providing reliable and flexible assessment of neuropsychological functioning in children aged three to twelve. The complete battery assesses five complex functional domains of EF. Two subtests were chosen to assess planning (Tower) and Verbal Fluency.

Tower

The NEPSY Tower task is modelled on Shallices' (1992) Tower of London task. The child is asked to rearrange three different coloured balls situated on three vertical pegs to reach a goal state, shown in a picture, in a prescribed number of moves without violating the rules (moving only one ball at a time, and only from one peg to another). This task is considered a measure of problem-solving and planning, but also requires working memory and inhibitory control. Hence the task measures several areas of Beebe & Gozal's (2002) model – working memory, behavioural inhibition, and analysis/synthesis,

Verbal Fluency

The Verbal Fluency test requires the child to generate words in response to semantic categories (animals, food/drink) and phonemic categories (words that begin with the letter 's' and 'f'). The number of words generated in 60 seconds is recorded. The task is a measure of Beebe & Gozal's (2002) reference to analysis/synthesis.

6.4.3.3. WISC

Two subtests from the WISC-III were used to measure processing speed.

Coding

In version A (children aged 6-7 years) the child has to mark rows of shapes with different lines according to a code as quickly as possible. In version B (children aged 8-16 years) the child must transcribe a digit-symbol code as quickly as possible. Two minutes are allocated to complete the task, with the number of correctly marked items scored.

Symbol Search

This also has a time limit of two minutes. Children are presented with rows of symbols and target symbols (one for children aged 6-7, two for children aged 8-16). The child must indicate (by marking a 'yes' or 'no' box) whether or not the target symbol appears in each row.

6.4.3.4. Automated Working Memory Battery

The Automated Working Memory Assessment (AWMA; Alloway, Gathercole, & Pickering, 2004) is a computer-based assessment that measures verbal short-term memory, visuo-spatial short-term memory, verbal working memory, and visuo-spatial working memory. Three tasks were chosen:

Backward Digit Recall

Almost identical to the Digit Recall task except the child must recall the digits in reverse sequence to that presented. Testing begins with a list length of two digits.

Spatial Span

The child views a picture of two arbitrary shapes, where the shape on the right has a red dot on it. The child identifies whether the shape on the right is the same as or opposite to the shape on the left. The shape with the red dot may also be rotated. At the end of each trial, the child has to recall the location of each red dot on the shape in sequence, by pointing to a picture with three compass points. Both the shapes and the compass points stayed on the computer screen until the child provided a response

6.4.4. Non-Executive Processes

The following task was also administered as a test of simple memory:

Automated Working Memory Assessment: Digit Recall

The child hears a sequence of digits (between 1 and 9) and has to recall the digits in the order presented. Testing begins with a list length of one digit. The child must successfully recall four (out of six) trials to proceed to the next level. Each subsequent level increases the number of digits by one up to a maximum of nine digits.

6.4.5. Measures: Behaviour

- Behavior Rating Inventory of Executive Function

Described in Chapter 5, section 5.4.3.1.

- Strengths and Difficulties Questionnaire

Described in Chapter 5, section 5.4.3.2.

6.4.6. Procedure

Ethical approval was obtained from the Ethics Committee in the School of Psychology, University of Southampton. NHS ethics was also obtained from Wiltshire Research Ethics Committee (REC reference 06/Q2008/51 – see Appendix B.5) for a study to use a sample of children with and without asthma and atopic dermatitis. However, only typically developing children could be recruited. As noted above, schools distributed letters to parents who then returned a freepost reply slip with their contact details to find out more about the study. Initial telephone contact with parents established whether the child was eligible to participate and to describe the study in detail. The first home visit was scheduled and families were sent two information sheets, one specific to the parent and another for the child (see Appendix B.2). At the first home visit informed written consent (Appendix B.3) was obtained from both the parent and child. The actigraph was given to the child who was instructed to wear the device until the second home visit. The oximeter was demonstrated to the parent and child, and the family were asked to attempt two nights of recording. The questionnaires were left with parents to be completed at a convenient time. The second home visit was usually scheduled for the following week when the neuropsychological testing was carried out. In some circumstances the neuropsychological testing was carried out at the first home visit. The study does not attempt to measure acute effects of sleep disturbance on EF, but makes the assumption that the week of actigraphy represents an average week for that child.

Parents were asked to provide a quiet room with table and chairs for the cognitive testing. The order tasks were presented in a standardised order so that the TEA-Ch, WISC, NEPSY, and AWMA were alternated in their presentation. The subtasks within the TEA-Ch could not be randomly presented because it requires the child to gain experience with certain tasks before progressing to others. The AWMA subtests were presented in the order specified by the computer. Total testing time was on average 1 hour 30 minutes, although the majority of tests lasted for about 1 hour 15 minutes and in some instances took nearly 2 hours.

6.4.7. Statistical Analyses

All analyses were performed in SPSS 16.0 for Macintosh (SPSS Inc, Chicago, Illinois). Data distributions were visually checked for normality by plotting histograms and conducting one sample Kolmogorov-Smirnov tests. Table 48 (Appendix B.6) shows the results of the one sample Kolmogorov-Smirnov tests for the sleep variables and the main aggregated dependent variables data (aggregated executive function score, and the total scores from the questionnaires). Mann Whitney *U* or independent t tests were conducted with gender as the IV and sleep, EF, and behaviour outcomes as the DV's. Pearson correlation coefficients were used to assess associations between age and all outcome measures. Linear regression was used to control for age and gender effects. Hierarchical forced entry regression was used to compare the effects of sleep quantity and sleep quality (with sleep efficiency and sleep minutes as the IV's) on global executive function as the DV. All tests are two-tailed unless otherwise indicated. As discussed in Chapter 5, Bonferroni corrections have not been applied to the study data.

In order to test the relationship between sleep disturbance and EF and behaviour problems, multivariate analysis of variance (MANOVA) was conducted with sleep high or low disturbance as the independent variable (IV) and the global executive function score and scores from the SDQ as the dependent variables (DV).

6.4.7.1. TEA-Ch

Raw scores are used in the analysis of TEA-Ch data. Executive functions develop rapidly during childhood and although normative scores are provided for the TEA-Ch, these are provided in age bands of two years. As the test is designed to provide a clinical assessment of a child, it was deemed appropriate to use raw scores for the sample. To control for gender and age effects, TEA-Ch raw scores were regressed (using linear regression) onto age and gender, the standardised residual scores from these regressions were used to analyse the relationship between sleep and TEA-Ch outcomes.

6.4.7.2. NEPSY

Raw scores are also used in the analysis of NEPSY data. Standardised scores are provided for the NEPSY but they do not account for possible gender effects. Linear regression was also used to regress NEPSY data onto age and gender and obtain

standardised residual scores that were used to analyse the relationship between sleep and NEPSY outcomes.

6.4.7.3. WISC

Standardised scores are used in the analysis of WISC data. The two WISC subtests used to calculate the processing speed index (Coding and Symbol Search) have two different versions: one for children aged 6-7 years, and another for children aged 8-16 years. The maximum possible score for the Coding subtests for children aged 6-7 years differs to that for children aged 8-16 years, thus it was necessary to use the normative scores. WISC scores are normalised for age with four-month bandings.

6.4.7.4. AWMA

Detailed information is not available regarding the standardised scores provided for the AWMA, hence standardised residual scores (obtained using the same method as the TEA-Ch and NEPSY) are used in the analysis of sleep and AWMA outcomes.

6.5. RESULTS

Complete data are not available for all children. The reasons for this include technical failures, parents not completing questionnaires, and children not completing tasks.

6.5.1. Age and Gender Effects

6.5.1.1. Actigraphy

Technical failures (of the actigraphs) occurred for eleven children, whereby the actigraph did not record any data. Eight of these cases underwent an additional week of actigraphy data collection; hence actigraphy data are only available for 56 children. Descriptive statistics for the actigraphy variables are shown in Table 49, Appendix B.6. Independent t tests revealed significant differences between boys and girls on some actigraphy variables. Girls had significantly longer sleep duration (total time from sleep-onset to sleep-offset) and more total sleep minutes compared to boys. Girls also had higher sleep efficiency, spent less time falling asleep, had fewer waking periods, and reduced activity compared to boys although these differences are not statistically significant. As shown in Table 52 (Appendix B.6), sleep duration was significantly associated with age – as would be predicted, increased age was associated with less sleep duration.

6.5.1.2. Children's Sleep Habits Questionnaire

Three parents did not complete the CSHQ, hence data are only available for 56 children. There were no significant differences (Mann Whitney *U* test) between boys and girls on any CSHQ subscales or the overall total CSHQ score (see Table 50, Appendix B.6). As shown in Table 52 (Appendix B.6), being older was significantly associated with fewer night wakings ($r = -.29$, $p < .05$). Age did not correlate with any other CSHQ subscales or the total CSHQ score. The mean CSHQ total score was 44.67. A one-sample t test ($t(56) = -10.32$, $p < .001$) showed this mean to be significantly lower than the CSHQ total mean (56.2) of the community sample reported by Owens et al. (2000) indicating that the sample represented a normal, healthy population.

6.5.1.3. Attention

Table 51 (Appendix B.6) shows the medians and interquartile range of TEA-Ch raw scores divided by gender. The performance of boys and girls on the TEA-Ch subtests was very similar. No significant differences between boys and girls were found. As expected, age was significantly correlated with all TEA-Ch outcomes (see Table 53, Appendix B.6) – older children were more likely to get higher scores.

6.5.1.4. NEPSY, AWMA, and WISC

Means and *SD* scores for the NEPSY, AWMA, and WISC subtests are shown in Table 54 (Appendix B.6). Girls scored significantly higher on the AWMA subtests of Backward Digit Recall and Spatial Span. Girls also scored higher on Verbal Fluency although this failed to reach significance. Table 53 (Appendix B.6) shows the Pearson correlation coefficients for age, NEPSY, AWMA raw scores and WISC standardised scores. Age was significantly associated with Verbal Fluency ($r = .56$, $p = .000$), Tower ($r = .27$, $p = .034$), Spatial Span ($r = .41$, $p = .005$), and Backward Digit Recall ($r = .30$, $p = .031$). In contrast, Digit Recall was not significantly correlated with age. WISC measures of Processing Speed are not correlated with age as these scores are already age adjusted.

6.5.1.5. Behavior Rating Inventory of Executive Function (BRIEF)

Age and gender comparisons were not made for BRIEF scores as they are normalised for both age and gender

6.5.1.6. Strengths & Difficulties Questionnaire (SDQ)

Mann Whitney U tests were used to compare SDQ scores of boys and girls. As shown in Table 55 (Appendix B.6), girls scored higher (*Mdn* = 2.00) than boys (*Mdn* = 1.5) on the Emotional Symptoms scale but this just failed to reach significance. No other significant differences were found.

6.5.2. Between-Task Associations

As shown in Table 53 (Appendix B.6) better performance on the Tower task was positively correlated with better performance on Verbal Fluency although this just failed to reach significance ($r = .25$, $p = .061$). Likewise, the association between Tower and processing speed just failed to reach significance ($r = .26$, $p = .051$). Higher scores on Verbal Fluency were significantly correlated with increased Backward Digit Recall ($r =$

.41, p = .002). Verbal Fluency performance was also significantly correlated with performance on the Spatial Span task (r = .38, p = .006) and Processing Speed Index (r = .29, p = .032). Digit Recall was significantly correlated with Backward Digit Recall (r = .37, p = .006) and Symbol Search (r = .30, p = .03). Backward Digit Recall was significantly correlated with Spatial Span performance (r = .35, p = .011) Coding (r = .28, p = .04), Symbol Search (r = .36, p = .009), and processing speed (r = .41, p = .002). Spatial Span showed a positive correlation with Symbol Search (r = .34, p = .013) and the Processing Speed Index (r = .32, p = .02).

6.5.3. Sleep and Executive Function Results

To examine whether performance on EF tasks was associated with actigraphic sleep variables, independent of age and gender effects, raw scores for TEA-Ch, NEPSY, and AWMA were regressed onto age and gender. The standardised residual scores from this regression analysis were used for Pearson correlation coefficient analyses to examine associations between sleep variables and EF.

Further analyses of the relationship between sleep and EF was conducted using aggregated z scores of the two main actigraphic sleep variables proposed to best represent sleep disturbance – total sleep minutes and sleep efficiency. A total sleep disturbance score was derived using the sum of standardised scores from the two actigraphic variables and the median was used to categorise children into two groups, high and low sleep disturbance. Hierarchical regression was used to test for the separate contribution of sleep quality and sleep quantity to global executive functioning.

6.5.3.1. TEA-Ch & actigraphy sleep variables

Associations between residual TEA-Ch scores and actigraphy sleep measures are shown in Table 7. Sleep duration was significantly associated with Score DT residual scores. Neither sleep duration nor sleep efficiency were significantly associated with any other TEA-Ch outcomes. A significant positive correlation is shown between sleep minutes and Score DT, indicating that more time spent asleep is associated with better performance on the divided attention task. Long wake episodes, wake after sleep onset, and activity index were all associated with Sky attention. Opposite Worlds was significantly correlated with sleep latency.

Table 7 Pearson correlation coefficients of actigraphy (n = 55) and TEA-Ch residual scores (n in brackets)

	1	2	3	4	5	6	7	11	12	13	14	15	16	17	18	19	20
Sleep duration	1.00																
Sleep minutes	**.64**	1.00															
Sleep efficiency	.11	**.78**	1.00														
Long wake episodes	.04	**-.64**	**-.91**	1.00													
Wake after sleep onset	.03	**-.70**	**-.98**	.94	1.00												
Sleep latency	-.21	-.20	-.15	.11	.14	1.00											
Activity index	-.15	**-.65**	**-.79**	**.75**	**.78**	.07	1.00										
Sky correct Z (58)	.17	.13	.10	.00	-.07	-.14	-.01	1.00									
Sky time Z (57)	-.09	-.24	-.21	.25	.23	.10	.24	.15	1.00								
Sky attention Z (57)	-.02	-.22	-.25	**.29**	**.27**	.14	.27	.09	**.74**	1.00							
Score Z (57)	-.02	-.02	-.02	-.05	.02	.06	-.03	.08	.17	.03	1.00						
Creature correct Z (56)	.18	.09	.02	.02	-.02	-.26	.01	**.27**	-.16	-.17	.10	1.00					
Creature time Z (55)	.12	.03	-.04	.06	.06	.14	.02	.03	.22	.25	-.05	-.05	1.00				
Sky DT Z (56)	-.09	-.05	-.02	-.09	.02	.23	.09	**-.38**	-.02	.02	-.14	**-.49**	.04	1.00			
Score DT Z (56)	.08	**.28**	.25	-.25	-.26	.03	-.15	.19	-.21	-.09	.18	.22	-.02	-.23	1.00		
Same Worlds Z (56)	.00	.14	.16	-.12	-.16	.16	-.23	.11	.09	.10	**-.28**	-.14	-.13	.03	-.01	1.00	
Opposite Worlds Z (56)	-.13	-.17	-.15	.08	.15	**.51**	.14	-.21	.05	.07	.08	**-.36**	.24	**.31**	-.16	**.39**	1.00

Significant correlations ($p < .05$) shown in bold script

Table 8 Pearson correlation coefficients of actigraphy (n = 55), NEPSY, AWMA, & WISC (n in brackets)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Sleep duration	1.00														
Sleep minutes	**.64**	1.00													
Sleep efficiency	.11	**.78**	1.00												
Long wake episodes	.04	**-.64**	**-.91**	1.00											
Wake after sleep	.03	**-.70**	**-.98**	**.94**	1.00										
Sleep latency	-.21	-.20	-.15	.11	.14	1.00									
Activity index	-.15	**-.65**	**-.79**	**.75**	**.78**	.07	1.00								
Coding (58)	**.43**	**.32**	.02	.02	.03	**-.29**	.00	1.00							
Symbol Search (58)	.10	.12	.07	-.05	-.07	-.16	-.03	.18	1.00						
Processing Speed (57)	**.36**	**.34**	.11	-.06	-.08	**-.30**	-.05	**.73**	**.76**	1.00					
Tower residual (57)	.25	**.34**	.24	-.17	-.19	.11	**-.33**	.16	.21	.26	1.00				
Verbal Fluency Z (58)	.21	**.28**	.18	-.13	-.16	**-.39**	-.01	**.33**	.14	**.30**	.12	1.00			
Digit Recall (53)	-.02	.07	.11	-.15	-.14	-.07	-.10	.00	**.30**	.22	-.09	.08	1.00		
Backward recall Z (53)	**.37**	**.31**	.21	-.18	-.18	-.27	.03	**.28**	**.28**	**.35**	.12	.26	**.33**	1.00	
Spatial Span Z (52)	-.04	.14	.16	-.10	-.17	-.06	-.16	.19	.24	.27	.04	.13	.11	.14	1.00

Significant correlations ($p < .05$) shown in bold scrip

6.5.3.2. NEPSY, AWMA, WISC, & actigraphy sleep variables

Table 8 shows the Pearson correlation coefficients for actigraphic sleep variables and NEPSY, AWMA, and WISC scores. Standardised residual scores are used for the Tower, Verbal Fluency, Backward Digit Recall, and Spatial Span. Raw scores are used in the correlations of Digit Recall (which were unchanged by the regression analysis), and standardised scores are used for WISC Coding, Symbol Search, and the Processing Speed Index.

Significant positive correlations are shown between Tower performance and both sleep minutes (r = .34, p = .012), and activity index (r = -.33, p = .015). There was an association between sleep efficiency and Tower but this failed to reach significance (r = .24, p = .074). Better Verbal Fluency scores were significantly correlated with increased sleep minutes (r-.28, p = .044) and decreased sleep latency (r = .39, p = .003). Performance on the Backward Digit Recall task showed a positive correlation with greater sleep duration (r = .37, p = .006) and increased sleep minutes (r = .29, p = .036). Spatial Span did not correlate significantly with any sleep variables, nor did Digit Recall.

Performance on the WISC subtest Coding was significantly associated with both sleep duration (r = .43, p = .001) and sleep minutes (r = .32, p = .018), Symbol Search was not significantly associated with any sleep variables. Processing speed was significantly associated with sleep minutes (r = .36, p = .006) sleep duration (r = .34, p = .012).

6.5.3.3. Total sleep disturbance and Global Executive Function

As noted above, a total sleep disturbance score was derived using the sum of the standardised scores of sleep efficiency and sleep minutes. The median was used to categorise children into two groups – high (n = 25) and low (n = 25) sleep disturbance. Independent t tests confirmed there was no difference between the two groups with regards to age (t(53) = 0.11, p > .05) or gender (t(53) = 1.48, p > .05). A Global Executive Function aggregate score (GEF) was derived from the sum of the following standardised scores (regressed onto age and gender): Sky attention, Score, Creature correct, Sky Search DT, Score DT, Opposite Worlds, Tower, Backward Digit Recall, Spatial Span, and Verbal Fluency. Processing speed was not included in the aggregated executive function score but examined in a separate analysis. A Higher GEF indicates

better performance on the EF tests. Independent t test analysis showed that children in the low sleep disturbance group had significantly higher GEF (M = 1.41, SD = 4.19) compared to children in the high sleep disturbance group (M = -1.58, SD = 4.48), t(51) = 2.448, p = .018. Figure 4 shows the 95% confidence intervals for the difference in Global Executive Function between children in the high and low sleep disturbance groups.

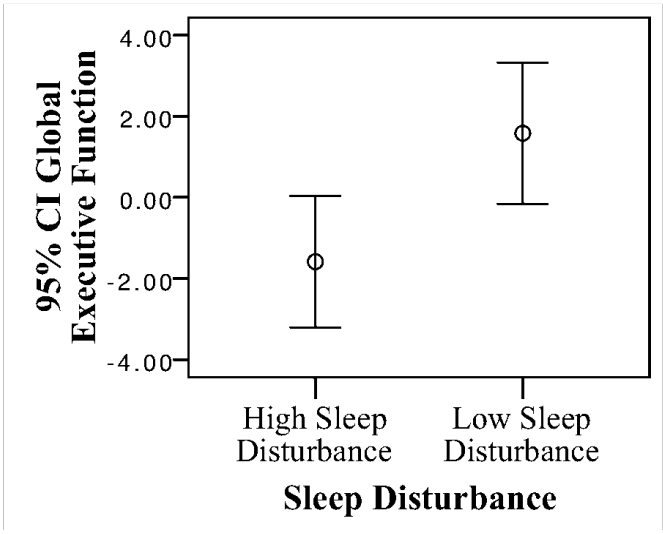

Figure 4 Global executive function of high and low sleep disturbance groups

6.5.3.4. Total sleep disturbance and processing speed

Independent t test showed that children in the high sleep disturbance group (n = 28) had significantly lower processing speed (M = 102.21) compared to children (n = 28) in the low sleep disturbance group (M = 109.64), t(53) = 2.30, p = .025.

6.5.3.5. Total sleep disturbance and non-executive function

Two of the subtests (Digit Recall and Same Worlds) administered to children were not EF tests. Independent t tests were used to compare the high and low sleep disturbance groups on these two subtests. There was no significant difference between the two groups on either Digit Recall (t(53) = .084, p = ns) or Same Worlds (t(53) = -.953, p = ns).

6.5.3.6. Effects of sleep quantity versus sleep quality on GEF

Linear regression was used to test the separate contribution of sleep quantity (sleep minutes) and sleep quality (sleep efficiency) on GEF. In the first model, sleep quality was entered in the first step and sleep quantity was entered in the second step. In the second model, the independent variables were entered in the reverse order, so that sleep quality was entered in the first step followed by sleep quality. Table 9 shows that in model 1, sleep quality was entered first and explained a non-significant proportion of the variance in GEF ($F(1,52) = 3.21$. $p > .05$). When sleep quantity was entered, a non-significant increment of 5% of the variance was explained ($F(1, 52) = 3.00$, $p > .05$), When sleep quality was entered alone it was not significant (beta = .25, $p < .08$). In model 2, when sleep quantity was entered first, a significant proportion of the variance in GEF was explained ($F(1, 52) = 6.45$, $p < .05$). Sleep quality did not significantly increase the proportion of variance in GEF ($F(1,52) = 0.00$, $p > .05$). When sleep quantity was entered alone it did show a significant effect (beta = .34, $p < .02$). Following the recommendations provided by Tabachnick & Fidell (1996, p.87), checks were run on the collinearity diagnostics in SPSS to determine if the conditioning index was greater than 30 for any root number and two variance proportions were greater than .50. These conditions were not met and therefore collinearity was not a problem. These results indicate that both sleep quality and quantity are important predictors of GEF, but that sleep quantity may be more important for executive functioning because it explained an additional unique proportion of the variance.

Table 9 Hierarchical multiple regression predicting GEF from sleep quality and sleep quantity

	R^2	R^2 change	B	SE B	Beta	F	*p*
Model 1							
Sleep quality	.06		-0.17	.12	-.03	3.21	.079
Sleep quantity	.12	.05	0.03	.16	.36	3.00	.089
Model 2							
Sleep quantity	.11		0.03	.02	.36	6.45	.014
Sleep quality	.12	.00	-0.17	.12	-.03	0.02	.888

6.5.4. Effects of Sleep on Behaviour: SDQ Results

6.5.4.1. SDQ and actigraphy correlations

The relationship between behaviour problems (as measured using the SDQ) and objective sleep measures (actigraphy) were assessed using Pearson correlation coefficients shown in Table 10. The Peer Problems subscale was significantly associated with shorter sleep duration (r = -.33, p = .02). Increased Conduct Problems was significantly associated with less sleep minutes (r = -.43, p = .001), lower sleep efficiency (r = -.33, p = .017), more long wake episodes (r = .28, p = .047), increased wake after sleep onset (r = .30, p = .033) and increased activity (r = .33, p = .016). Longer sleep latency was associated with increased Hyperactivity (r = .27, p = .05) and Emotional Symptoms (r = .35, p = .01). Actigraphy sleep variables did not correlate with SDQ ratings of the pro-social scale.

6.5.4.2. SDQ and CSHQ

Correlations between SDQ subscales and CSHQ subscales are shown in Table 11. A number of significant associations are shown and all correlations were in the expected direction – increased parental reports of behaviour problems were associated with increased parental reports of sleep problems. Emotional Symptoms were significantly associated with the total CSHQ score (r = .56, p < .001) and all subscales. Increased parental reports of Conduct Problems were significantly correlated with the overall total CSHQ score (r = .62, p < .001) as well as the following subscales: Bedtime Resistance (r = .41, p = .003), Sleep Onset Delay (r = .46, p = .001), Sleep Duration (r = .58, p < .001), Daytime Sleepiness (r = .61, p < .001). Parental reports of hyperactivity were significantly correlated with the total CSHQ score (r = .48, p = .001), and the following subscales: Sleep Duration (r = .45, p = .001), Parasomnias (r = .28, p = .034), and Daytime Sleepiness (r = .41, p = .014). Hyperactivity was correlated with Bedtime Resistance (r = .24, p = .06) but this failed to reach significance. Peer Problems was significantly correlated with Bedtime Resistance (r = .28, p = .045) but not the total CSHQ score or any other subscales. The total SDQ score was significantly correlated with the total CSHQ score (r = .70, p < .001) and all subscales apart from Sleep Anxiety.

Table 10 Pearson correlation coefficients of actigraphy (n = 56) and SDQ (n = 55)

	1	2	3	4	5	6	7	8	9	10	11	12	13
Sleep duration	1.00												
Sleep minutes	.67	1.00											
Sleep efficiency	.14	**.78**	1.00										
Long wake episodes	.01	**-.64**	**-.91**	1.00									
Wake after sleep onset	.00	**-.70**	**-.99**	**.94**	1.00								
Sleep latency	-.24	-.23	-.16	.12	.14	1.00							
Activity index	-.17	**-.65**	**-.79**	**.75**	**.78**	.09	1.00						
Emotional Symptoms	.04	-.04	-.15	.27	.18	**.35**	.11	1.00					
Conduct Problems	-.20	**-.43**	**-.33**	**.28**	**.30**	.09	**.33**	**.31**	1.00				
Hyperactivity	-.12	-.20	-.12	.08	.11	**.27**	.09	**.31**	**.55**	1.00			
Peer Problems	-.33	-.12	.02	-.09	-.07	**.34**	.01	.16	.12	.12	1.00		
Pro-social	.04	.15	.03	-.10	-.04	.09	-.18	.06	**-.52**	-.14	-.01	1.00	
Total SDQ	-.12	-.16	-.11	.08	.11	**.40**	.10	**.59**	**.63**	**.82**	**.44**	-.12	1.00

Significant correlations, $p < .05$, shown in bold script

Table 11 Pearson correlation coefficients of CSHQ (n = 53) and SDQ (n = 52)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Bedtime Resistance	1.00														
Sleep Onset Delay	**.40**	1.00													
Sleep Duration	**.29**	**.53**	1.00												
Sleep Anxiety	**.59**	**.38**	.12	1.00											
Night Wakings	**.46**	**.30**	.16	**.51**	1.00										
Parasomnias	**.36**	**.28**	**.28**	**.37**	**.50**	1.00									
Sleep-Disordered breathing	-.04	.12	.13	-.01	.08	.18	1.00								
Daytime Sleepiness	.23	**.31**	**.34**	.16	.15	-.03	.20	1.00							
Total CSHQ	**.70**	**.64**	**.62**	**.64**	**.64**	**.60**	**.28**	**.60**	1.00						
Emotional Symptoms	**.36**	**.37**	**.44**	**.42**	**.30**	**.29**	**.43**	**.39**	**.61**	1.00					
Conduct Problems	**.43**	**.47**	**.59**	.19	.25	.18	.17	**.60**	**.65**	**.28**	1.00				
Hyperactivity	.24	**.29**	**.45**	-.05	.12	**.28**	.13	**.41**	**.48**	.26	**.53**	1.00			
Peer Problems	.24	.17	.13	.08	.14	.23	.24	.25	.32	.08	.11	.08	1.00		
Pro-social	-.16	-.26	-.22	.11	.14	.18	.04	**-.38**	-.19	.12	-.52	-.11	.02	1.00	
Total SDQ	**.40**	**.45**	**.53**	.23	**.32**	**.35**	**.28**	**.59**	**.71**	**.54**	**.63**	**.81**	**.39**	-.07	1.00

Significant correlations, $p < .05$, shown in bold script

6.5.4.3. SDQ of high and low sleep disturbance groups

Median SDQ scores of children with high and low sleep quality are presented in Table 12. Some of the subscales were not normally distributed so Mann Whitney U tests were used to compare the groups. Children with high sleep disturbance had significantly higher rates of conduct problems compared to children with low sleep disturbance. No other differences were found between the groups.

Table 12 Mann Whitney U tests of SDQ by high and low sleep disturbance

	Low Sleep Disturbance (n=25)		High Sleep disturbance (n=27)		*U* test	
	Median	*IQR*	Median	*IQR*	*U*	*p**
Emotional Symptoms	2.00	4.00	2.00	6.00	317.00	.704
Conduct Problems	0.00	2.00	3.00	3.00	165.50	.001
Hyperactivity	4.00	4.00	5.00	5.00	265.00	.181
Peer Problems	1.00	3.00	2.00	3.00	272.00	.216
Pro-social scale	9.00	2.00	9.00	3.00	259.50	.140
Total SDQ	9.00	6.00	12.00	12.00	252.50	.119

*Asymptotic significance

6.5.4.4. BRIEF and actigraphy

Pearson correlation coefficients between BRIEF subscales and actigraphy sleep variables are shown in Table 57 (Appendix B.6). Sleep duration was significantly associated with Initiate, Plan/Organise, Organisation of Materials, Metacogntion, and GEC: Parents reported fewer problems in children who had longer sleep durations. A negative correlation was found between sleep duration and working memory but this just failed to reach significance (p = .054). Significant negative correlations were found between sleep minutes and Plan/Organize. A negative correlation between sleep minutes and GEC just failed to reach significance (p = .069).

6.5.4.5. BRIEF and CSHQ

Associations between subscales of the BRIEF and CSHQ are shown in Table 58 (Appendix B.6). Bedtime Resistance was significantly correlated with Inhibit, Shift, Emotional Control, Behavioural Regulation, and total BRIEF. Sleep Onset Delay was significantly associated with all BRIEF subscales except Shift and Monitor. Sleep Duration was significantly correlated with all BRIEF subscales except Initiate and Organisation of materials. No significant correlations were found between BRIEF subscales and the CSHQ subscales of Sleep Anxiety, Night Wakings, and Parasomnias. A significant positive correlation as shown between sleep disordered breathing and Behavioral Regulation. Daytime Sleepiness was significantly associated with all BRIEF subscales, except Shift, which just failed to reach significance (p = .059). The total CSHQ score was significantly associated with Inhibit, Shift, Emotional Control, Working Memory, Monitor, Behavioural Regulation, Metacognition, and the total BRIEF.

6.5.4.6. BRIEF scores of high and low sleep disturbance groups

BRIEF scores of children with high and low sleep quality are presented in Table 56 (Appendix B.6). To explore the relationship between behaviour and sleep, multivariate analysis of variance (MANOVA) was calculated with sleep disturbance (as described above) as the independent variable (age and gender were not controlled for as the BRIEF scores are standardised). Table 13 shows that the multivariate effect of sleep disturbance was not significant ($F(10,43) = 1.17$, $p > .05$).

Table 13 F ratios and effect sizes for univariate main effects of sleep quality on BRIEF subscales

Source		Mean Square	df	*F*	*P*
Multivariate	Sleep quality $\lambda = .764$		10	1.17	ns
Univariate					
Sleep quality	Inhibit	253.50	1	2.65	ns
	Shift	48.17	1	.42	ns
	Emotional Control	18.96	1	.18	ns
	Initiate	88.17	1	.85	ns
	Working Memory	52.02	1	.37	ns
	Plan/Organize	150.00	1	1.13	ns
	Org. Materials	48.17	1	.42	ns
	Monitor	39.19	1	.42	ns
	Behavioural Regulation	140.17	1	1.38	ns
	Metacognition	3.63	1	.03	ns
Error	Inhibit	95.74	52		
	Shift	114.80	52		
	Emotional Control	107.05	52		
	Initiate	10411	52		
	Working Memory	142.03	52		
	Plan/Organize	132.68	52		
	Org. Materials	113.74	52		
	Monitor	90.65	52		
	Behavioural Regulation	101.93	52		
	Metacognition	109.61	52		

6.5.5. Comparison of Actigraphy and CSHQ

As shown in Table 52, (Appendix B.7) few significant associations were found between actigraphy sleep variables and parent-reported sleep variables (CSHQ). Actigraphy total sleep minutes was significantly correlated with CSHQ Sleep Duration, indicating that parents were good at estimating the amount their child slept.

6.5.6. Oximetry Results

Overnight home pulse oximetry data were only available for 23 children and the descriptive statistics are shown in Table 14. Fourteen children did not want to undergo the assessment and data on eight children were lost due to the limited memory capacity of the oximeters. In four cases, the oximeter failed due to a blown fuse. Of the 33 oximetry reports that were collected, ten were excluded due to inadequate data, leaving only 23 complete reports.

Table 14 Means and *SD* of oximetry values

	Mean	*SD*	Minimum	Maximum
SpO2 nadir	90.28	76.60	70.50	98.00
SpO2 baseline	97.39	1.17	94.65	99.14
Desaturation 4	0.79	1.33	0.00	6.34
Delta 12s index	0.28	0.10	0.17	0.59
Time below 95%	3.48	9.69	0.00	43.17

As described in section 6.4.2.2, a probable diagnosis of SDB was determined by abnormal parameters on two or more oximetry values and a possible diagnosis of SDB on the basis of one abnormal parameter (with the exception of abnormal nadir alone). Applying the criteria to the subsample with oximetry data available, two children were categorised as having a possible diagnosis of SDB.

6.6. DISCUSSION

6.6.1. Study Aim: Obtaining Pulse Oximetry Data

One aim of the study was to obtain pulse oximetry data on this sample of non-referred children. Oximetry data were only available for 23 children and only two children in this subsample reached the threshold for possible SDB diagnosis. The subsample of 23 children with oximetry data is assumed to be representative of the total sample, hence it is concluded that SDB is likely to be minimal in the complete sample of 59 children. A larger proportion of children with oximetry data may have enabled a comparison of EF in children with and without possible/probable SDB.

6.6.2. Study Aim: To examine the specific effects of sleep disturbance on executive function.

6.6.2.1. Beebe & Gozal's model of OSA and prefrontal dysfunction

The results from this study support the model of prefrontal dysfunction proposed by Beebe & Gozal (2002) to account for the pattern of cognitive deficits seen in patients with OSA. In the model, both sleep disruption and intermittent hypoxia are proposed as factors that affect the brain, and consequently daytime functioning, specifically executive functioning. However, the model does not clarify the relative importance of each of these factors affecting prefrontal cortical dysfunction. There is a large body of literature showing that deficits in cognitive functioning can be related to OSA and SDB. However, there is also research that demonstrates similar cognitive deficits in individuals with sleep disturbance but no known OSA or SDB. For example, Horne (1988) has proposed that the prefrontal cortex is particularly sensitive to the effects of sleep disturbance, but he makes no mention of OSA as a vehicle for this sleep disruption. Hence, the question remains as to whether the effects upon EF from OSA and SDB are caused by sleep disruption or intermittent hypoxia, or a combination of both. To the best of my knowledge, no study has compared EF in children with SDB to that of children with sleep disturbance but no SDB. It is possible that sleep disruption and intermittent hypoxia have similar effects on prefrontal functioning, and a combination of the two results in greater deficits. Further research is needed to clarify these issues.

Hypothesis 1: Children with higher sleep disturbance, in the absence of sleep-disordered breathing, will have poorer overall executive functioning compared to children with low sleep disturbance.

One aim of this study was to determine whether high sleep disturbance (defined as poor quality of sleep and shorter sleep duration), in the absence of sleep-disordered breathing, is associated with deficits in the executive functions highlighted by Beebe & Gozal (2002) as susceptible to the effects of obstructive sleep apnoea. Children were grouped into high and low sleep disturbance using a median split of the aggregated sleep quality and sleep quantity scores. In support of hypothesis 1, children with high sleep disturbance had significantly lower EF compared to children in the low sleep disturbance group. EF was characterised using an aggregate score derived from the sum of ten subtests, which measured sustained attention, divided attention, verbal inhibition, behavioural inhibition, planning, verbal working memory, spatial working memory, and verbal fluency. The difference between the two group means was 3.17, this equates to a large effect size of .75.

Hypothesis 2. Non-executive measures of cognition (digit recall) will not be associated with sleep disturbance (defined as shorter sleep time and lower sleep efficiency).

Hypothesis 2 was supported as neither of the simple cognitive measures – digit recall and Same Worlds – were significantly different between the high and low sleep disturbance groups.

6.6.3. Study Aim: To explore the relationship between sleep disturbance and processing speed.

Hypothesis 3: Children with high sleep disturbance will have lower processing speed compared to children with low sleep disturbance.

In support of hypothesis 3, a significant deficit in processing speed was also found in the group with higher sleep disturbance. Previous research has shown that children with mild sleep-disordered breathing have lower processing speed (Hill et al., 2006). This study demonstrated significantly lower processing speed in children with high sleep disturbance in the absence of SDB.

6.6.4. Study Aim: To Compare the Relative Importance of Sleep Quality Versus Sleep Quantity.

One aim of this study was to examine whether deficits in EF are differentially affected by sleep quality or sleep quantity. As noted in the introduction, the literature examining sleep disturbance and executive functioning has yet to clarify the relative importance of sleep quantity and sleep quality to EF. It was hypothesised that deficits in EF would be associated with increased sleep disturbance (as measured using sleep quantity and sleep quality), in the absence of sleep-disordered breathing. It was not hypothesised whether either of these sleep factors would have a greater impact on EF. A hierarchical linear regression was conducted and showed that both sleep quality and sleep quantity were important predictors of EF, however, sleep quantity explained an additional unique proportion of the variance suggesting that quantity of sleep may have a greater impact upon EF compared to quality of sleep.

6.6.5. Study Aim: To Examine Associations between Sleep Disturbance and Parental Report of Behaviour.

Hypothesis 4. Parental reports of behaviour problems (as measured using the SDQ) will be associated with actigraphy measured sleep disturbance (defined as shorter sleep time and lower sleep efficiency) and parental reports of sleep problems. In particular, children with high sleep disturbance will have higher rates of conduct problems.

This study adds support to previous findings of sleep disturbance and behaviour problems in children. Smedje, Broman, & Hetta (2001) found an association between higher parental reports of emotional symptoms (using the SDQ) and difficulties falling asleep. They also demonstrated an association between increased conduct problems and greater bedtime resistance. In this study, children who spend longer falling asleep (as measured using actigraphy and parental report) had increased rates of emotional symptoms and hyperactivity. More conduct problems were also reported in children who had increased rates of Bedtime Resistance (as measured using the CSHQ), and shorter sleep times and lower sleep efficiency as measured using actigraphy. The findings were also supported by the univariate analysis showing that children in the high sleep disturbance group had higher reports of conduct problems. Sleep duration as measured using actigraphy, did not correlate with SDQ subscales. However, previous research by Aronen et al. (2000) found that sleep duration as measured using actigraphy was associated with teacher reports of externalizing symptoms, but not parental reports

of externalizing problems. Sleep latency was significantly associated with parental reports of attention and aggressive/delinquent behaviour problems, as did this study. Parental reports of sleep were also significantly associated with the SDQ. Total sleep disturbance as measured using the CSHQ was significantly associated with elevated rates of emotional symptoms, conduct problems, and hyperactivity. This is in line with the findings from Study 1. These findings are also consistent with previous research examining parental reports of sleep and behaviour. Higher rates of behaviour problems in children (as measured using the SDQ) have previously been associated with parental reports of sleep disturbance (Smedje, Broman, & Hetta, 2001). Furthermore, ADHD symptoms have also been associated with parental reports of sleep problems (Chervin et al., 2002).

Similar results were obtained for the BRIEF questionnaire. The MANOVA failed to find an effect of sleep disturbance (as measured using actigraphy) on BRIEF subscales, although there were some significant correlations between BRIEF subscales and actigraphy. In contrast, parental reports of sleep using the CSHQ correlated well with BRIEF subscales. Overall, higher sleep disturbance (total CSHQ score) was associated with increased reports almost all BRIEF subscales.

6.6.6. Summary of Chapter 6

In a sample of healthy, typically developing children assumed to be free of any SDB, this study demonstrated that children with high sleep disturbance, defined as shorter sleep duration and poorer quality sleep, had poorer Global Executive Function compared to children with low sleep disturbance. Hierarchical regression analysis suggests that sleep quantity, as measured using actigraphy, may be a better predictor of EF compared to sleep quality. There was some indication that behaviour problems were more frequent in children with high sleep disturbance, however these results were inconclusive.

CHAPTER 7 STUDY 3
SLEEP AND NEUROPSYCHOLOGICAL FUNCTIONING IN CHILDREN WITH CYSTIC FIBROSIS

7.1. INTRODUCTION

Chapter 6 examined sleep disturbance and neuropsychological functioning in a sample of healthy, typically developing children aged 6-12 years. The findings presented in that chapter demonstrate that children with increased sleep disturbance, as defined by less sleep time and lower sleep efficiency, perform more poorly on tests of EF. Scores from the EF tests were aggregated to give an overall level of executive functioning, rather than relying on individual test scores.

Chapter 6 emphasised the model of prefrontal dysfunction, proposed by Beebe & Gozal (2002), as a theoretical basis for determining which executive functions should be affected by sleep disturbance. However, the model proposed by Beebe & Gozal (2002) was developed to account for the deficits in EF seen in patients with obstructive sleep apnoea. In Chapter 6, the participants were children with no known sleep-disordered breathing problems: oximetry data on a sub-sample of these children showed two possible cases of SDB in the sample. The model proposed by Beebe & Gozal (2002) accounts for the pattern of EF deficits found in OSA patients by suggesting that two factors prevent sleep-related restorative processes: blood gas abnormalities from hypoxia and disruption of sleep architecture. However, the model does not specify the relative importance of the two causative factors. Research has shown that children (and adults) with no known SDB may also exhibit deficits in EF that can be associated with sleep disruption (Sadeh et al., 2002; Steenari et al., 2003).

The literature has yet to clearly address what the proportional effects of hypoxia and disruption of sleep architecture are upon EF. If EF deficits are shown in children without SDB, it is possible that blood gas abnormalities in children with SDB are not the cause of EF deficits. Rather, it may be that disruption to the sleep architecture that may result in the executive dysfunction. Alternatively, SDB and disruption to sleep architecture may have an additive effect on deficits in EF, if this is correct, then EF deficits in children with SDB would be greater than EF deficits seen children with disrupted sleep but no hypoxia. The aim of Study 3 is to examine these proposals by

repeating the methodology and procedures used in Study 2 with a sample of children who may be at risk of blood gas abnormalities from SDB. As discussed in Chapter 4 (section 4.3.2.2), children with cystic fibrosis are at risk of sleep disturbance from nocturnal hypoxia, hypoventilation, and chronic cough. Actigraphy studies have shown that children with CF have lower sleep efficiency and more frequent awakenings compared to controls (Amin et al., 2005) and polysomnography studies have shown reduced sleep efficiency and less REM sleep (Naqvi et al., 2008).

I conducted a comprehensive search of the literature using a variety of search engines (OVID, Web of Knowledge, PubMed, and Google Scholar) inputting the following search keywords: children AND cystic fibrosis AND executive function OR executive functioning OR cognition OR behaviour. No studies were found that have examined executive functioning or other cognitive abilities in children with CF. This is not surprising given that CF is a fatal disorder with a life expectancy of 31 years – parents and clinicians are likely to be most concerned with the physical well-being of children with CF rather than their cognitive functioning. However, given that CF children are at risk of sleep disturbance, they are also at risk of the cognitive and behavioural deficits associated with sleep disturbance. This chapter will firstly examine within-group differences in sleep disturbance and EF in children with CF, and then examine between-group differences in sleep and EF of CF children and the healthy controls reported in Study 1. Based on the findings of Study 2, it is expected that children with CF will exhibit similar patterns of association between sleep and cognition and behaviour. It is hypothesised that children with CF will have greater sleep disturbance compared to the TD sample examined in Study 2. As a consequence, children with CF will, compared to healthy children, children with CF will have poorer performance on EF tasks compared to typically developing children.

7.2. AIMS OF STUDY 3

1. To explore whether children with cystic fibrosis exhibit the same pattern of associations shown in Chapter 6 between sleep disturbance and EF in typically developing children
2. To determine whether children with CF have increased sleep disturbance compared to the healthy controls examined in Study 1.

3. To explore how nocturnal hypoxia may contribute to EF deficits caused by sleep disturbance, as proposed by Beebe & Gozal (2002). Specifically, the aim is to determine whether the effects of sleep disturbance on neuropsychological functioning are greater when nocturnal hypoxia is also present.

7.3. HYPOTHESES

1. CF children with high sleep disturbance (the independent variable defined as poorer sleep efficiency and less total sleep time) will have poorer global EF (the dependent variable) compared to CF children with low sleep disturbance.
2. Processing speed (the dependent variable) will be lower in CF children with high sleep disturbance (the independent variable) compared to CF children with low sleep disturbance.
3. Children with CF will have significantly lower sleep duration and sleep efficiency and more wake after sleep onset (the dependent variables), as measured using actigraphy, compared to children without CF (with group – CF or TD as the independent variable).
4. Global executive function (the dependent variable) will be lower in children with CF compared to controls (with group as the independent variable).
5. There will be a greater incidence of nocturnal hypoxia (dependent variable) in children with CF compared to controls (independent variable = group).
6. The presence of nocturnal hypoxia and sleep disturbance (the independent variables) will increase a child's susceptibility to neuropsychological deficits (the dependent variable) compared to the presence of sleep disturbance alone.

7.4. METHOD

7.4.1. Participants

Children aged 6 – 13 years were recruited via the cystic fibrosis clinic at Southampton General Hospital. The age range was extended slightly for this study to maximise participant numbers whilst minimising the impact that puberty can have on sleep. Puberty often starts later in children with CF. The clinic provides full or shared care for patients in Southampton, Poole, Winchester, Swindon, and Dorchester. A CF nurse or consultant telephoned parents to give brief details of the study. Letters were sent out to parents who could not be contacted by telephone. Further telephone contact was made

by myself if the families agreed to be contacted. The clinic database had 49 children aged between 6 and 13 years eligible to take part (a further five children were not eligible to take part due to a history of ADHD or learning difficulties). Children were also excluded if they had an acute exacerbation of chronic bronchitis or significant illness at the time of the study. The CF clinic contacted thirty-six families by telephone and eleven families by letter (two families had two children eligible to take part). Twelve families (twelve children) contacted by telephone did not want further information. Of the eleven families contacted by letter, five returned a reply slip giving permission for the researcher to contact them with further information. Of the 29 families (31 children) that did want further info, 2 families (3 children) decided not to participate. Two families could not be included in the study as they lived too far away.

The final sample consisted of 26 children aged 6 years 2 months to 12 years 10 months (mean age 9 years 3 months). The sample consisted of 13 boys and 12 girls who did not differ with regards to age ($t(1,25) = -0.63$, df = 25, $p > .05$). Two children were siblings. The majority of children lived in a two-parent household (22), 1 child lived with a single parent, 2 children had parents who were separated or divorced and the parent of 1 child was widowed. Table 15 shows the educational background statistics of the parents of the sample.

Table 15 Educational achievements of parents of children with CF

	Mothers	Fathers
No qualifications	3 (12%)	3 (12%)
GCSE/O Levels	5 (19%)	5 (19%)
A levels/NVQ/Highers	38 (44%)	5 (19%)
Degree	2 (8%)	2 (8%)
Postgraduate degree	3 (3%)	5 (19%)
Missing	3 (11%)	6 (23%)

7.4.2. Measures: Sleep

7.4.2.1. Actigraphy

Actigraphy is described in detail in Chapter 5 (section 5.3.2.1). Children were instructed to wear the actigraphs continuously for seven days and nights (mean number of nightly recordings = 6.6, range = 4 – 9 nights). Data were averaged across the number of nights. The main variables of interest in Study 3 are defined as:

1. Total sleep minutes: number of minutes scored as sleep from sleep-onset to sleep-offset.
2. Sleep efficiency: The percentage of time (in minutes) scored as sleep from the first sleep-onset period to the last sleep-offset period.
3. Number of waking episodes lasting more than 5 minutes, from sleep-onset to sleep-offset.

7.4.2.2. Pulse oximetry

Pulse oximetry is described in Chapter 6 (section 6.4.2.2). The likelihood of sleep-disordered breathing was determined using the same reference values as in Study 2.

7.4.2.3. Children's Sleep Habits Questionnaire

As described in Chapter 5 (section 5.3.2.2), the Children's Sleep Habits Questionnaire (CSHQ) is a validated sleep-screening instrument designed to assess a variety of sleep behaviours and sleep habits in children.

7.4.3. Materials: Executive Function and Non-Executive Function

The same battery of neuropsychological tests was used that were administered in Study 1. Full descriptions are given in Chapter 6 (section 6.4.3) of the tests that were used:

7.4.4. Measures: Behaviour

1. Behaviour Rating Inventory of Executive Function

Described in Chapter 5 (section 5.3.4.1).

2. Strengths and Difficulties Questionnaire

Described in Chapter 5 (section 5.3.4.2).

7.4.5. Procedure

Ethical approval was initially obtained from the Ethics Committee in the School of Psychology, University of Southampton. NHS ethical approval was obtained from Isle of Wight, Portsmouth and South East Hampshire Research Ethics Committee (REC reference number 08/H051/26, see Appendix C.1). NHS R&D approval was obtained from Southampton General Hospital (RHM CHI0459). Initial telephone contact with parents established whether the child was eligible to participate and to describe the study in detail. The first home visit was scheduled and families were sent two information sheets, one specific to the parent and the other for the child (See Appendix C.2). Parents were asked to telephone if the child became unwell prior to the first visit. At the first home visit informed written consent was obtained from both the parent and child (Appendix C.3). The actigraph was given to the child who was instructed to wear the device until the second home visit. The oximeter was demonstrated to the parent and child, and they were asked to attempt two or three nights of recording. The questionnaires were left with parents to be completed at a convenient time. The second home visit was usually scheduled for the following week when the neuropsychological testing was carried out. In some circumstances the neuropsychological testing was carried out at the first home visit. The study does not attempt to measure acute effects of sleep disturbance on EF, but makes the assumption that the week of actigraphy represents an average week for that child.

Parents were asked to provide a quiet room with table and chairs for the cognitive testing. The tasks were presented in a randomised order so that the TEA-Ch, WISC, NEPSY, and AWMA were alternated in their presentation. The subtasks within the TEA-Ch could not be randomly presented because it requires the child to gain experience with certain tasks before progressing to others. The AWMA subtests were presented in the order specified by the computer. Total testing time was on average 1 hour 15 minutes, although some children took slightly longer to complete all the tests.

7.4.6. Statistical Analyses

Pearson correlation coefficients were used to assess associations between age and all outcome measures. Data distributions were visually checked for normality by plotting histograms and conducting one sample Kolmogorov-Smirnov tests. Table 60 (Appendix C.4) shows the results of the one sample Kolmogorov-Smirnov tests for the sleep variables and the main aggregated dependent variables data (aggregated executive

function score, and the total scores from the questionnaires) which were all non-significant. In order to test for gender effects, Mann Whitney U or independent t tests were conducted with gender as the independent variable and sleep, EF, and behaviour and sleep outcomes as the dependent variables. Initially, the raw EF scores were used in the analyses but in the subsequent analyses the residual scores were used. Linear regression was used to control for age and gender effects. Hierarchical forced entry regression was used to compare the effects of sleep quantity and sleep quality on global executive function, with sleep minutes and sleep efficiency as the IV's and GEF as the DV. Independent t tests and multivariate analysis of variance were used to compare differences between high and low sleep disturbance groups. Sleep disturbance (high or low) was the IV, and the DV's were scores from the parental questionnaires (SDQ, BRIEF). All tests are two-tailed unless otherwise indicated.

7.4.6.1. Multiple testing

As discussed in Chapter 5, Bonferroni corrections have not been used to adjust for multiple testing. The issue of whether or not to adjust for multiple testing is a complex one that has been widely debated. Perneger (1998) argues that such adjustments are overly conservative and unnecessary unless one is searching for significant associations in the absence of pre-established hypotheses.

7.4.6.2. TEA-Ch

Raw scores are used in the analysis of TEA-Ch data. Executive functions develop rapidly during childhood and although normative scores are provided for the TEA-Ch, these are provided in age bands of two years. As the test is designed to provide a clinical assessment of a child, it was deemed appropriate to use raw scores for the sample. To control for gender and age effects, TEA-Ch raw scores were regressed (using linear regression) onto age and gender, the standardised residual scores from this regression were used to analyse the relationship between sleep and TEA-Ch outcomes.

7.4.6.3. NEPSY

Raw scores are also used in the analysis of NEPSY data. Standardised scores are provided for the NEPSY but they do not account for possible gender effects. Linear regression was also used to regress NEPSY scores onto age and gender and obtain standardised residual scores that were used to analyse the relationship between sleep and NEPSY outcomes.

7.4.6.4. WISC

Standardised scores are used in the analysis of WISC data. The two WISC subtests used to calculate the Processing Speed Index (Coding and Symbol Search) have two different versions: one for children aged 6-7 years, and another for children aged 8-16 years. The maximum possible score for the Coding subtests for children aged 6-7 years differs to that for children aged 8-16 years, therefore it was necessary to use the normative scores that are provided. WISC scores are normalised for age with four-month bandings.

7.4.6.5. AWMA

Detailed information is not available regarding the standardised scores provided for the AWMA, hence standardised residual scores (obtained using the same method as the TEA-Ch and NEPSY) are used in the analysis of sleep and AWMA outcomes.

7.5. RESULTS

7.5.1. Age and Gender Effects in Children with CF

7.5.1.1. Actigraphy

One child lost the actigraph and it was not possible to repeat the actigraphy recording with that child, therefore complete data were only available for 25 children. There were no technical failures. Independent t tests revealed no significant differences between boys and girls on any actigraphy variables (Table 61, Appendix C.4) hence any effects of gender can be discounted in subsequent analyses. As shown in Table 63 (Appendix C.4), sleep duration, both actigraphy and parent report, were significantly associated with age, as would be predicted, increased age was associated with less sleep duration.

7.5.1.2. Children's Sleep Habits Questionnaire

Table 64 (Appendix C.4) shows the medians and *IQR* for CSHQ subscales by gender. Girls had a significantly greater number of Night Wakings and higher Daytime Sleepiness compared to boys. There were no other significant differences between boys and girls on the CSHQ subscales. The total CSHQ score was higher in girls compared to boys, although this failed to reach significance.

7.5.1.3. Attention

Table 64 (Appendix C.4) shows the medians and *IQR* of TEA-Ch raw scores divided by gender. The performance of boys and girls on the TEA-Ch subtests was very similar: there were no significant differences between boys and girls. As expected, age was significantly correlated with all TEA-Ch outcomes (see Table 66, Appendix C.4) – older children were more likely to get higher scores.

7.5.1.4. NEPSY, AWMA, and WISC

Means and *SD* scores for the NEPSY, AWMA, and WISC subtests are shown in Table 65 (Appendix C.4). There were no significant differences between boys and girls for any of the variables. Table 66 (Appendix C.4) shows the Pearson correlation coefficients for age, NEPSY, AWMA raw scores and WISC standardised scores. Age was significantly associated with Verbal Fluency ($r = .62$, $p < .001$), Spatial Span ($r = .44$, $p = .002$), and Backward Digit Recall ($r = .56$, $p = .001$). An association between age and Tower failed to reach significance ($r = .34$, $p = .096$). In contrast, Digit Recall was not significantly correlated with age. WISC measures of processing speed are not correlated with age as these scores are already age adjusted

7.5.1.5. Strengths & Difficulties Questionnaire (SDQ)

Mann Whitney U tests were used to compare SDQ scores of boys and girls with CF. As shown in Table 67 (Appendix C.4), there were no differences between boys and girls on any subscales or the total score of the SDQ.

7.5.2. Between-Task Associations

As shown in Table 66 (Appendix C.4) higher scores on Verbal Fluency were significantly correlated with increased Backward Digit Recall ($r = .49$, $p = .01$). Backward Digit Recall was significantly correlated with Spatial Span performance ($r = .51$, $p = .01$).

7.5.3. Sleep and Executive Function in Children with CF

The relationship between sleep and EF in children with cystic fibrosis was examined using the same methodology employed for the healthy controls examined in Chapter 6. To control for age and gender effects, raw scores for TEA-Ch, NEPSY, and AWMA were regressed onto age and gender and the standardised residual scores were used for

Pearson correlation coefficient analyses examining the associations between sleep variables and EF.

Further analyses of the relationship between sleep and EF was conducted using aggregated z scores of the two main actigraphic sleep variables – total sleep minutes and sleep efficiency. A total sleep disturbance score was derived using the sum of standardised scores from those two actigraphic variables and the median was used to categorise children into two groups, high and low sleep disturbance. Hierarchical regression was used to test for the separate contribution of sleep quality and sleep quantity to global executive functioning.

7.5.3.1. TEA-Ch & actigraphy sleep variables

Associations between residual TEA-Ch scores and actigraphy sleep measures are shown in Table 16. Longer sleep latency was significantly associated with better performance on Opposite Worlds and Creature Correct. There were no other significant associations between TEA-Ch residual scores and sleep duration, sleep minutes, long wake episodes, wake after sleep onset, or activity index. However, some correlations were in the expected direction but just failed to reach significance. Better Sky timing scores were associated with increased sleep minutes (r = -.37, p = .07).

Table 16 Pearson correlation coefficients of actigraphy and TEA-Ch residual scores in children with CF (n = 25)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Sleep duration	1.00																
Sleep minutes	**.47**	1.00															
Sleep efficiency	-.05	**.83**	1.00														
Long wake episodes	.29	**-.62**	**-.90**	1.00													
Wake after sleep	.15	**-.78**	**-.99**	**.93**	1.00												
Sleep latency	-.10	-.32	-.30	.23	.28	1.00											
Activity index	.12	**-.69**	**-.86**	**.88**	**.87**	.31	1.00										
Sky correct Z	.09	.05	.03	.01	-.02	.14	-.05	1.00									
Sky time Z	-.20	-.37	-.32	.25	.28	.16	.16	-.27	1.00								
Sky attention Z	-.02	-.21	-.25	.21	.23	.20	.12	-.06	**.59**	1.00							
Score Z	.07	-.27	-.34	.34	.34	-.32	.26	.03	.09	.22	1.00						
Creature correct Z	-.01	.12	.17	-.10	-.17	**-.44**	-.11	.01	.09	.27	.04	1.00					
Creature time Z	-.08	.01	.04	-.06	-.06	-.16	-.18	-.20	**.61**	.21	.12	.15	1.00				
Sky DT Z	.17	.21	.06	-.06	-.04	.14	-.09	.08	-.37	-.32	.10	**-.78**	-.25	1.00			
Score DT Z	.25	.17	.13	.00	-.10	-.31	-.03	.36	-.39	-.15	.36	.08	-.16	.23	1.00		
Same world Z	-.06	-.12	-.09	.11	.07	.17	-.03	-.29	**.60**	.09	-.21	-.21	**.52**	-.06	-.31	1.00	
Opposite world Z	-.10	-.15	-.11	.09	.08	**.43**	-.02	-.10	**.58**	.12	-.27	**-.40**	.38	.02	-.36	**.90**	1.00

Significant correlations, $p < .05$, shown in bold script

Table 17 Pearson correlation coefficients of actigraphy, NEPSY, AWMA, & WISC in children with CF (n = 25)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Sleep duration	1.00														
Sleep minutes	**.47**	1.00													
Sleep efficiency	-.05	**.83**	1.00												
Long wake episodes	.29	**-.62**	**-.90**	1.00											
Wake after sleep	.15	**-.78**	**-.99**	**.93**	1.00										
Sleep latency	-.10	-.32	-.30	.23	.28	1.00									
Activity index	.12	**-.69**	**-.86**	**.88**	**.87**	.31	1.00								
Coding	-.06	-.03	.00	-.24	-.03	-.03	-.06	1.00							
Symbol Search	-.03	-.10	.00	-.03	.02	-.26	-.03	.33	1.00						
Processing Speed Index	-.07	-.09	-.01	-.16	.00	-.17	-.05	**.81**	**.81**	1.00					
Tower Z	.22	-.03	-.21	.17	.23	-.13	.16	.25	-.11	.09	1.00				
Verbal Fluency z	-.17	-.09	.04	-.13	-.06	-.10	-.06	.18	-.10	.05	.07	1.00			
Digit Recall	.21	-.37	**-.52**	**.62**	**.55**	.04	**.51**	-.30	-.07	-.23	.02	.25	1.00		
Backward Digit Recall Z	-.03	**-.40**	-.39	.30	.37	-.11	.30	.04	-.03	.00	-.02	.24	.24	1.00	
Spatial Span Z	.08	-.15	-.24	.29	.26	-.11	.21	-.02	.16	.08	.02	-.17	.12	.37	1.00

Significant correlations, $p < .05$, shown in bold script

7.5.3.2. NEPSY, AWMA, WISC, & actigraphy sleep variables

Table 17 shows the Pearson correlation coefficients for actigraphic sleep variables and NEPSY, AWMA, and WISC scores. Standardised residual scores are used for the Tower, Verbal Fluency, Backward Digit Recall, and Spatial Span. Normative scores are used for WISC Coding, Symbol Search, and Processing Speed Index.

An unexpected significant negative correlation is shown between Backward Digit Recall and sleep minutes (r = -.40, p =.04). Also unexpected was the finding that better performance on Digit Recall was associated with poorer sleep efficiency (r = -.52, p = .01), more long wake episodes, and more wake after sleep onset.

7.5.3.3. Total sleep disturbance and global executive functioning

As noted above, a total sleep disturbance score was derived using the sum of the standardised scores of sleep efficiency and sleep minutes. The median was used to categorise children into two groups – high (n = 13) and low (n = 12) sleep disturbance. Independent t tests confirmed there was no difference between the two groups with regards to age, $t(23) = 0.44$, $p > .05$, or gender, $t(23) = 0.61$, $p > .05$. A Global Executive Function aggregate score (GEF) was derived from the sum of the following standardised scores (regressed onto age and gender): Sky attention, Score, Creature Correct, Sky Search DT, Score DT, Opposite Worlds, Tower, Backward Digit Recall, Spatial Span, and Verbal Fluency). Processing speed was not included in the aggregated EF score but examined in a separate analysis. A Higher GEF indicates better performance on the EF tests. Independent t test analysis showed that GEF was not significantly different between the high sleep disturbance (M = 0.80, SD = 2.73) and low sleep disturbance group (M = -0.87, SD = 5.19), $t(23) = 1.02$, $p >.05$. However this difference is in the expected direction and would suggest an effect size of 1.6 *SD*.

7.5.3.4. Total sleep disturbance and processing speed

Children in the high sleep disturbance group (n = 13) had lower processing speed scores (M = 102.85, SD = 13.82) compared to children (n = 12) in the low sleep disturbance group (M = 113.25), but this just failed to reach significance in an independent t test, $t(23) = -1.88$, $p = .07$.

7.5.3.5. Total sleep disturbance and non-executive function

Two of the subtests (Digit Recall and Same Worlds) administered to children were not EF tests. Independent t tests were used to compare the high and low sleep disturbance groups on these two subtests. Unexpectedly, children in the high sleep disturbance group had significantly better digit recall scores (M = 31.08, SD = 4.61) compared to children in the low sleep disturbance group (M = 25.42, SD = 1.98), $t(23) = 3.93$, p = .01. There was no significant difference between the two groups on Same Worlds performance, $t(23) = .816$, $p > .05$.

7.5.4. Effects of Sleep on Behaviour in Children with CF: SDQ Results

7.5.4.1. SDQ and actigraphy correlations

The relationship between behaviour problems (as measured using the SDQ) and objective sleep measures (actigraphy) was assessed using Pearson correlation coefficients shown in Table 18. Neither sleep duration nor total sleep minutes were significantly associated with any SDQ subscales. Lower sleep efficiency was associated with increased Conduct Problems (r = -.46, p = .02), and increased Hyperactivity although this failed to reach significance (r = .35, p = .09). The total SDQ was also significantly correlated with sleep efficiency (r = .46, p = .02). Increased wake after sleep-onset was significantly correlated with increased Conduct Problems (r = .46, p = .02) the total SDQ (r = .47, p = .02), and increased activity (r = .33, p = .02). Shorter sleep latency was associated with higher pro-social scores (r = .27, p = .05) and Emotional Symptoms (r = .52, p = .01).

7.5.4.2. SDQ and CSHQ

Correlations between SDQ subscales and CSHQ subscales are shown in Table 19. Sleep Onset Delay was significantly associated with the pro-social scale of the SDQ (r = .44, p = .03). CSHQ Sleep Duration was significantly correlated with Conduct Problems (r = .47, p = .02), Pro-social Scale (r = -.65, p = .001) and the total SDQ (r = .41, p = .04). Increased Parasomnias was significantly associated with the total SDQ score (r = .48, p =.02). Parental report of sleep-disordered breathing was significantly associated with Peer Problems (r = .47, p = .02). Both Daytime Sleepiness and the total CSHQ score were significantly correlated with all SDQ subscales apart from the Pro-Social Scale.

Table 18 Pearson correlation coefficients of actigraphy and SDQ in children with CF (n = 25)

	1	2	3	4	5	6	7	8	9	10	11	12	13
Sleep duration	1.00												
Sleep minutes	.47	1.00											
Sleep efficiency	-.05	**.83**	1.00										
Long wake episodes	.29	**-.62**	**-.90**	1.00									
Wake after sleep onset	.15	**-.78**	**-.99**	**.93**	1.00								
Sleep latency	-.10	-.32	-.30	.23	.28	1.00							
Activity index	.12	**-.69**	**-.86**	**.88**	**.87**	.31	1.00						
Emotional Symptoms	.18	.04	-.12	.12	.15	.28	.07	1.00					
Conduct Problems	.18	-.33	**-.46**	.28	**.46**	.21	.26	.21	1.00				
Hyperactivity	.16	-.19	-.35	.30	.37	.16	.26	.20	**.61**	1.00			
Peer Problems	-.13	-.33	-.32	.27	.30	.14	.17	.16	.10	.34	1.00		
Pro-social	-.04	.24	.25	-.08	-.23	**-.52**	-.07	-.03	**-.67**	**-.56**	-.16	1.00	
Total SDQ	.18	-.28	**-.46**	.36	**.47**	.30	.29	**.53**	**.77**	**.85**	**.54**	**-.56**	1.00

Significant correlations, $p < .05$, shown in bold script

Table 19 Pearson correlation coefficients of CSHQ and SDQ in children with CF (n=24)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Bedtime Resistance	1.00														
Sleep Onset Delay	.18	1.00													
Sleep Duration	-.04	.36	1.00												
Sleep Anxiety	.24	-.08	.17	1.00											
Night Wakings	.37	.09	-.06	.25	1.00										
Parasomnias	.19	.15	.19	.04	.26	1.00									
Sleep-Disordered Breathing	.10	-.09	.24	.13	-.08	**.55**	1.00								
Daytime Sleepiness	.13	.11	.29	.02	**.49**	**.47**	**.43**	1.00							
Total CSHQ	**.41**	.33	**.52**	.31	**.54**	**.67**	**.52**	**.83**	1.00						
Emotional Symptoms	.09	.01	.10	.03	.04	**.42**	.16	**.48**	**.41**	1.00					
Conduct Problems	-.12	.01	**.47**	.05	.14	.29	.11	**.45**	**.43**	.21	1.00				
Hyperactivity	-.13	.22	.32	.24	.02	.38	.27	**.45**	**.47**	.20	**.65**	1.00			
Peer Problems	.15	.08	.21	.22	.11	.20	**.47**	**.44**	**.45**	.16	.07	.33	1.00		
Pro-social	.28	**-.44**	**-.65**	.08	.03	-.01	.06	-.30	-.30	-.03	**-.66**	**-.55**	-.13	1.00	
Total SDQ	-.03	.13	**.41**	.20	.11	**.48**	.35	**.66**	**.64**	**.55**	**.76**	**.85**	**.52**	**-.55**	1.00

Significant correlations, $p < .05$, shown in bold script

7.5.4.3. SDQ of high and low sleep disturbance groups

Mann Whitney U tests were used to compare SDQ scores of children with high (n = 12) and low sleep quality (n = 13). No significant differences were found (see Table 71 (Appendix C.4).

7.5.4.4. BRIEF and actigraphy

Pearson correlation coefficients between BRIEF subscales and actigraphy sleep variables are shown in Table 68 (Appendix C.4). Sleep duration was not significantly associated with any BRIEF subscales. Increased sleep minutes was significantly correlated with lower scores on the Initiate subscale. Both sleep efficiency and wake after sleep-onset were significantly associated with lower scores on Inhibit, Emotional Control, Initiate, Working Memory, Monitor, Behavioural Regulation and the total BRIEF score. Sleep latency was significantly associated with Monitor.

7.5.4.5. BRIEF and CSHQ

Associations between subscales of the BRIEF and CSHQ are shown in Table 69 (Appendix C.4). Sleep Duration was significantly correlated with Inhibit, Emotional Control, Plan/Organize, Initiate, Monitor, Behavioural Regulation, Metacognition, and total BRIEF. The Parasomnias subscale of the CSHQ was significantly correlated with Initiate, Working Memory, Plan/Organize, Monitor, Behavioural Regulation, Metacognition, and the total BRIEF score. Daytime Sleepiness was significantly associated with all CSHQ subscales but not Organisation of Materials. The total CSHQ score was significantly correlated with all BRIEF subscales and total score.

7.5.4.6. BRIEF scores of high and low sleep disturbance groups

BRIEF scores of children with high (n = 13) and low (n = 12) sleep quality are presented in Table 72. To explore the relationship between behaviour and sleep, multivariate analysis of variance (MANOVA) was calculated with sleep disturbance (as described above) as the independent variable (age and gender were not controlled for as the BRIEF scores are standardised). Table 20 shows that the multivariate effect of sleep disturbance was not significant, $F(11,13) = 1.13$, $p > .05$.

Table 20 *F* ratios and effect sizes for univariate main effects of sleep quality on BRIEF subscales

Source		Mean Square	df	*F*	*p*
Multivariate	Sleep quality $\lambda = .511$		11	1.13	ns
Univariate					
Sleep quality	Inhibition	93.85	1	0.69	ns
	Shifting	6.24	1	0.04	ns
	Emotional Control	7.06	1	0.05	ns
	Initiate	225.60	1	1.39	ns
	Working memory	88.95	1	0.57	ns
	Planning	48.30	1	0.33	ns
	Organising	173.25	1	1.77	ns
	Monitoring	5.47	1	0.04	ns
	Behavioural regulation	26.75	1	0.18	ns
	Metacognition	34.54	1	0.28	ns
Error	Inhibition	135.40	23		
	Shifting	139.57	23		
	Emotional Control	130.00	23		
	Initiate	162.76	23		
	Working memory	156.86	23		
	Planning	148.73	23		
	Organising	97.71	23		
	Monitoring	138.00	23		
	Behavioural regulation	146.72	23		
	Metacognition	122.40	23		

7.5.4.7. BRIEF and SDQ

The relationship between BRIEF and SDQ subscales is shown in Table 70 (Appendix C.4). Parental reports of behaviour problems by using the SDQ was highly correlated with parental reports of executive function behaviour problems using the BRIEF. Conduct Problems Hyperactivity, Pro-Social Scale, and the total SDQ score were significantly associated with all BRIEF subscales apart from Organisation of Materials. Emotional Symptoms correlated significantly with Monitor. Higher Peer Problems was significantly associated with Inhibit, Shift, Working Memory, Plan/Organize, Monitor, Metacognition, and the total BRIEF score.

7.5.5. Comparison of Actigraphy and CSHQ

As shown in Table 63 (Appendix C.4), few significant associations were found between actigraphy sleep variables and parent-reported sleep variables (CSHQ). Actigraphy sleep duration and sleep minutes were significantly correlated with parent report of Sleep Anxiety (CSHQ).

7.6. OXIMETRY RESULTS

Overnight home pulse oximetry data were only available for 18 children; the descriptive statistics for these data is shown in Table 21. In four cases, the finger probe had fallen off during the night. The recording from one child was not used because the actigraphy data from that night indicated that the child was awake for a significant proportion of the night. In three cases data were not sufficient to be analysed.

Table 21 Means and *SD* of oximetry values in children with CF

	Mean	*SD*	Minimum	Maximum
SpO2 Nadir	84.56	10.24	59.00	98.00
SpO2 Mean	96.38	3.32	83.71	99.11
Desaturation Index	2.51	5.23	0.00	22.91
Number of desaturations	19.53	38.78	0.00	171.00
Delta 12s Index	0.49	0.34	0.18	1.18
Time Below 95	4.55	8.72	0.00	26.65

As described in section 7.4.2.2, a probable diagnosis of SDB was determined by abnormal parameters on two or more oximetry values and a possible diagnosis of SDB on the basis of one abnormal parameter (with the exception of abnormal nadir alone). Applying the criteria to the subsample with oximetry data available, 3 children were classified as having a possible diagnosis of SDB, and 4 children were classified as having a probable diagnosis of SDB.

7.7. DISCUSSION

Study Aim: To explore whether children with cystic fibrosis exhibit the same pattern of associations shown in Chapter 6 between sleep disturbance and EF in typically developing children.

7.7.1.1. Sleep results

There were no significant differences between the actigraphy variables of boys and girls with cystic fibrosis. This is in contrast to the study in Chapter 6 of healthy typically developing children where girls had significantly longer sleep durations and longer total sleep minutes. Sleep efficiency in the control girls was also higher than in the control boys, although this just failed to reach significance ($p = .059$). Parent report of sleep problems (CSHQ) in children with CF was not identical for boys and girls. As reported by parents, girls had significantly more night wakings and more daytime sleepiness compared to boys. Furthermore, the total CSHQ was higher for girls, although this just failed to reach significance. These results are in contrast to the CSHQ results for healthy boys and girls, which showed no significant differences.

7.7.1.2. Executive function results

Boys and girls with CF did not differ on any of the TEA-Ch subtests. In the healthy controls, the only significant difference was that girls had better Sky timing scores. A comparison of the NEPSY, AWMA, and WISC scores shows there were no significant gender differences in children with CF. In contrast, healthy girls performed significantly better on both the Backward Digit Recall task and Spatial Span task compared to healthy boys. Verbal Fluency was also higher in healthy girls compared to healthy boys although this just failed to reach significance ($p = .07$).

7.7.1.3. Sleep disturbance and executive function

The results of the analyses examining associations between sleep and EF in children with CF are somewhat different to the results of the healthy controls reported in Chapter 6. Performance on the two NEPSY tasks was not associated with actigraphy sleep variables although in the healthy sample there was an association between better performance on the Tower and Verbal Fluency tasks and increased sleep minutes. In children with CF, Digit Recall was significantly associated with sleep efficiency, although this was a negative relationship, with poorer sleep efficiency being associated with better Digit Recall. In contrast, there was no association between digit recall and actigraphy sleep variables in the healthy control sample. Backward Digit Recall was significantly associated with sleep duration and sleep minutes in the healthy sample, but in children with CF there was a negative relationship. Better Backward Digit Recall was significantly associated with less sleep minutes.

Hypothesis 1: CF children with high sleep disturbance (defined as poorer sleep efficiency and less total sleep time) will have poorer global EF compared to CF children with low sleep disturbance

Global Executive Function (GEF) was examined in the CF children using the same methodology used for the healthy control sample reported in Chapter 6. Children were divided into high and low sleep disturbance groups using a median split of the aggregated sleep quality (sleep efficiency) and quantity (total sleep minutes) score.
In the typically developing sample, a significant difference was found between the high and low sleep disturbance groups. Children who slept better (i.e. slept for longer and had better quality sleep) had higher Global Executive Function (an aggregate of the main EF test scores). Using the same analyses in the sample of children with CF, children in the low sleep disturbance group had a lower GEF scores compared to children in the high sleep disturbance group, however the difference was not significant.

Hypothesis 2: Processing speed will be lower in CF children with high sleep disturbance compared to CF children with low sleep disturbance

In the sample of healthy children reported in Chapter 6, longer sleep times (both total actual minutes sleep and sleep duration) were associated with better processing speed performance. This association was not repeated in the CF sample because processing speed was not significantly associated with any actigraphy sleep variables. Furthermore,

in the univariate analysis of sleep groups, healthy children in the low sleep disturbance group had significantly higher processing speed compared to children in the high sleep disturbance group. However, as shown above in section 7.6.3.4, in children with CF, hypothesis 2 was not supported because although processing speed was higher in children with low sleep disturbance this failed to reach significance.

7.7.1.4. Sleep and Behaviour Results in Children with CF

In the control sample, less sleep time was significantly associated with increased rates of conduct problems. Although there was a similar association in the CF children, it was not significant. In the healthy sample, better sleep efficiency was associated with less parental report of conduct problems and this association was also found in the sample of CF children. Sleep efficiency was also associated with the total SDQ in the CF sample: children who slept less well had higher rates of behaviour problems. The number of long wake episodes was associated with conduct problems in the healthy sample but this association was not found in the CF sample. The number of minutes spent awake after sleep-onset was associated with increased rates of behaviour problems in healthy children and also in children with CF. Children with CF also showed an association between the total SDQ score and number of minutes awake after sleep-onset. Finally, in the healthy sample, children who spent longer falling asleep had higher parental reports of emotional symptoms, hyperactivity, and peer problems. In the CF sample, none of these associations were found, however, children who fell asleep quicker were more social (as reported by parents).

Total sleep disturbance as measured using the CSHQ was significantly associated with elevated rates of emotional symptoms, conduct problems, and hyperactivity, and total behaviour problems in the typically developing sample. A similar pattern of associations was found for children with CF; children who were rated by their parents as having more emotional symptoms, conduct problems, and hyperactivity were also more likely to be have higher total CSHQ scores. Examining the subscales in detail, higher rates of conduct problems in the healthy sample was associated with Bedtime Resistance, Sleep Onset Delay, Sleep Duration, and Daytime Sleepiness. For children with CF, only Sleep Duration and Daytime Sleepiness were associated with conduct problems. Hyperactivity was associated with Sleep Duration, Parasomnias, and Daytime Sleepiness in healthy children, but in the CF sample, only Daytime Sleepiness showed a significant relationship with Hyperactivity (Parasomnias just failed to reach

significance, $r = .38$, $p = .07$). A multivariate analysis of variance (MANOVA) showed that in healthy children, conduct problems were significantly more frequent in children in the high sleep disturbance group. The MANOVA of the CF sample did not show this difference.

The pattern of associations for the BRIEF questionnaire and actigraphy data were quite different in the children with CF compared to the healthy controls. In fact, although there were several correlations between various subscales of the BRIEF and actigraphy variables in both the control sample and the CF sample, none of the significant associations were identical. Any significant correlations in the healthy children were not found in the CF children, and vice versa, none of the significant associations found in the CF sample had been found in the control sample. Of particular note were the significant relationships between both sleep efficiency and wake after sleep-onset, and the total BRIEF score in children with CF. The total BRIEF score in healthy children was only significantly correlated with sleep duration.

Associations between parent reports of sleep (CSHQ) and behaviour problems using the BRIEF in the two samples showed similarities as well as differences. Both Bedtime Resistance and Sleep Onset Delay were significantly correlated with several BRIEF subscales as well as the total BRIEF score, but these associations were not repeated in CF sample. In both the healthy children and the CF children, parents who reported more problems with their child's sleep duration, also reported higher rates on nearly all BRIEF subscales and the total BRIEF score. Neither Sleep Anxiety nor Night Wakings were associated with behaviour problems in either sample. There were no associations between BRIEF subscales and either Parasomnias or Sleep-Disordered Breathing in the healthy children. However, in the children with CF, increased rates of Parasomnias was significantly correlated with the Metacognitive subscales of the BRIEF (Initiate, Working Memory, Plan/Organize, Organisation of Materials) and the total BRIEF score but not with the Behavioral Regulation subscales. In both samples, parent reports of Daytime Sleepiness was associated with most BRIEF subscales, and, the total CSHQ score was significantly correlated with almost all BRIEF subscales in the typically developing sample and all BRIEF subscales in the CF sample. The MANOVAs that were conducted to determine whether children with high sleep disturbance had significantly higher parent reports of EF behaviour problems failed to find an effect of sleep disturbance in both the healthy sample and the children with CF.

7.7.2. Conclusions

Comparing the results of the healthy children with that of the children with CF, it is notable that although there were similarities between the two groups, there were also some striking differences between the two sets of results. Of particular interest is the disparity in the processing speed results. In the typically developing sample, processing speed was better in children with longer sleep times, and this relationship was supported in the univariate analysis of the high and low sleep disturbance groups – children in the low sleep disturbance group had better processing speed scores than children in the high sleep disturbance group. In contrast, children with CF did not have better processing speed if they slept for longer, nor was there a significant difference in the processing speed of children in the high and low sleep disturbance groups. The reason for this discrepancy in the results is unclear, although it is quite likely that the smaller sample size in the CF group has contributed to these findings.

Another notable difference in the results concerns the associations between EF and actigraphy sleep data. In the control sample, increased sleep minutes was associated with better performance on three of the key EF tasks: Tower, Verbal Fluency and Backward Digit Recall tasks. However, these associations were not replicated in the CF sample, in stark contrast, children with CF did worse on Backward Digit Recall if they had longer sleep times! This may also be a consequence of the small sample size.

The results of the behaviour and sleep data in the two samples were more comparable. Although there were differences, overall the two samples showed similar patterns of associations. Higher rates of behaviour problems were found in children with poorer sleep, particularly on parent reports.

The remainder of this chapter compares the statistical data from the typically developing children reported in Chapter 6, with the data presented here from the sample of children with CF.

7.8. Between-subjects Analyses of Children with and without CF

The following sections will present between-group analyses of the two groups (children with and without CF) in a similar order to the results already presented. All variables from the combined dataset (children with and without CF) were checked for normal distributions by conducting one sample Kolmogorov-Smirnov tests (see Tables 76 -81, Appendix C.4). Normally distributed data were analysed with independent t tests, in all other cases Mann Whitney U tests were conducted. Firstly I shall examine whether there are any differences between the two groups with regards to their sleep patterns, then differences in EF performance, and then examine between-group differences in reports of behaviour.

7.8.1. Sleep in Children with and without CF

Actigraphy data for children with CF and healthy controls were compared using independent t tests. As show in Table 22, there were no significant differences in any actigraphy sleep variables of children with and without CF. Parental report of sleep problems in children with and without CF is shown in Table 23. Parents of children with CF reported higher rates of Daytime Sleepiness in their children compared to parents of children who do not have CF.

Table 22 Actigraphy means and *SD* of children with and without CF

	Controls (n=52)		CF (n=25)		*t* test (df=75)	
	Mean	*SD*	Mean	*SD*	*t*	*p*
Sleep duration	566.44	38.23	563.41	33.22	0.339	.735
Total sleep minutes	480.96	57.82	473.45	53.34	0.547	.586
Sleep efficiency	85.32	8.01	84.61	8.68	0.355	.724*
Sleep latency	49.78	31.89	42.38	20.34	1.059	.293
Long wake episodes	4.92	2.75	4.81	2.65	0.165	.869
Activity index	46.63	12.70	45.43	15.31	0.363	.718
Wake after sleep onset	82.90	44.02	86.26	48.00	-0.305	.761

* Sleep efficiency was not normally distributed, however, as the t-test was non-significant, a non-parametric test would not have yielded a different result.

Table 23 Mann Whitney U tests of CSHQ of children with and without CF

	Controls (n=49)		CF (n=24)		U test	
	Median	*IQR*	Median	*IQR*	*U*	*p**
Bedtime Resistance	7.00	2.00	6.00	1.00	527.00	.437
Sleep Onset Delay	2.00	1.00	1.50	1.00	565.00	.775
Sleep Duration	4.00	3.00	3.00	2.00	437.00	.059
Sleep Anxiety	4.00	0.00	4.00	2.00	496.00	.182
Night Wakings	3.00	1.00	3.00	1.00	542.00	.530
Parasomnias	9.00	3.00	8.00	2.00	512.50	.365
Sleep-Disordered Breathing	3.00	1.00	3.00	1.00	571.50	.823
Daytime Sleepiness	11.00	4.00	13.00	6.00	402.00	.028
Total CSHQ	43.00	9.00	45.00	11.00	528.50	.484

* Asymptotic Significance

7.8.2. Attention in Children with and without CF

Performance of on the TEA-Ch subtests of healthy controls and children with CF is shown in Table 24. No significant differences were found between the two groups on any subtests.

Table 24 Mann Whitney U tests of TEA-Ch subtests in children with and without CF

	Controls (n=50)		CF (n=25)		U test*	
	Median	*IQR*	Median	*IQR*	*U*	*p*
Sky correct	19.00	2.00	20.00	2.00	558.00	.423
Sky timing	5.20	2.26	4.70	2.18	545.00	.369
Sky attention	3.87	2.10	3.90	2.32	592.50	.715
Score	8.00	2.00	10.00	3.00	489.50	.118
Creature correct	6.00	2.00	6.00	2.00	579.50	.590
Creature timing	4.33	1.08	3.85	2.60	555.50	.435
Sky DT	1.02	3.36	0.25	2.50	562.50	.482
Score DT	15.50	4.00	17.00	6.00	538.00	.326
Same Worlds	29.00	4.61	26.90	9.80	524.50	.259
Opposite Worlds	36.05	2.37	34.50	10.35	536.50	.320

* Asymptotic Significance

7.8.3. NEPSY, AWMA, and WISC Scores in Children with and without CF

Means and *SD* scores for the NEPSY, AWMA, and WISC subtests are shown in Table 25. Independent t tests showed no significant differences between healthy control children and children with CF.

Table 25 Group comparisons of NEPSY, AWMA, & WISC: children with and without CF

	Controls (n=52)		CF (n=25)		U test	
	Median	*IQR*	Median	*IQR*	*U*	*p*
Tower	11.00	2.00	11.00	4.00	589.50	.687
Verbal Fluency	47.50	18.00	50.00	17.00	564.50	.496
Digit recall	26.00	4.00	28.00	5.00	529.50	.279
Backward Digit Recall	10.00	5.00	12.00	9.00	532.50	.296
Spatial Span	18.00	9.00	18.00	7.00	618.00	.937
Symbol Search	12.00	4.00	13.00	4.00	560.00	.325
	Mean	*SD*	Mean	*SD*	*t*	*p*
Coding	10.38	2.88	10.32	3.13	-1.077	.285
Processing speed	106.04	12.95	107.84	14.55	-0.549	.585

7.8.4. Global Executive Function in Children with and without CF

Global Executive Function (GEF) was compared in healthy controls and children with CF by replicating the analyses examining GEF in high and low sleep disturbed groups in both the controls and children with CF. EF scores were regressed onto age and gender (and reverse scored where necessary so that a high GEF represented better performance) and the standardised residuals used in the analysis. Independent t test analysis showed that the GEF of healthy controls (M = 0.04, SD = 4.23) and children with CF (M = -0.05, SD = 3.79) was not significantly different, $t(1,75) = .087$, $p > .05$.

7.8.5. Behaviour in Children with and without CF

7.8.5.1. SDQ in healthy children and children with CF

SDQ scores of healthy control children and children with CF are presented in Table 26. Parent report of behaviour problems using the SDQ was examined using Mann-Whitney

U-tests (the total SDQ score was normally distributed but subscales were not, see Table 76, Appendix C.4). There were no significant differences between the two groups.

Table 26 Mann Whitney U tests of SDQ scores: control and CF children

	Controls (n = 48)		CF (n = 25)		*U* test	
	Median	*IQR*	Median	*IQR*	*U*	*p*
Emotional Symptoms	2.00	5.00	2.00	2.00	540.00	.479
Conduct Problems	1.50	3.00	1.00	2.00	536.50	.447
Hyperactivity	4.00	4.00	4.00	3.00	502.00	.251
Peer Problems	2.00	3.00	1.00	3.00	520.00	.336
Pro-social scale	9.00	3.00	9.00	4.00	562.00	.648
Total SDQ	10.00	10.00	8.00	9.00	494.00	.217

7.8.5.2. BRIEF parental reports in children with and without CF

Parent report of behaviour problems using the BRIEF was examined using Mann-Whitney U-tests (several subscales were not normally distributed, see Table 78, Appendix C.4). As shown in Table 27, there were no significant differences between the two groups.

Table 27 Mann Whitney U tests of BRIEF scores in control and CF groups

	Controls (n = 50)		CF (n = 25)		*U* test	
	Median	*IQR*	Median	*IQR*	*U*	*p*
Inhibit	51.00	12.00	46.00	13.00	502.50	.168
Shift	52.00	16.00	45.00	12.00	487.00	.120
Emotional Control	54.00	15.00	51.00	16.00	556.50	.441
Initiate	52.50	16.00	53.00	15.00	601.50	.791
Working memory	55.50	19.00	54.00	17.00	557.50	.448
Plan/organize	54.00	22.00	51.00	21.00	564.00	.493
Organisation of materials	52.50	18.00	58.00	15.00	556.00	.438
Monitor	52.00	11.00	47.00	18.00	471.50	.084
Behavioural Regulation	52.50	15.00	51.00	12.00	507.50	.186
Metacognition	54.50	14.00	55.00	11.00	607.00	.840
Total BRIEF	53.00	13.00	53.00	11.00	550.00	.399

7.8.6. Comparison of Oximetry Data in Children with and without CF

As discussed in the introduction, one aim of the study was to examine whether children with CF have nocturnal hypoxia, and if so, whether this contributes to the effects of sleep disturbance on EF. Mann-Whitney U tests were used to compare the oximetry values obtained for children with and without CF. As shown in Table 28, there were no significant differences in oximetry between the two groups. The delta index was higher in children with CF compared to controls but just failed to reach significance.

Table 28 Means and *SD* of oximetry values in control and CF children

	Controls (n = 22)		CF (n = 16)		*U* test	
	Median	*IQR*	Median	*IQR*	*U*	*p**
SpO_2 Nadir	90.50	14.75	86.50	13.13	155.50	.251
SpO_2 mean	1.46	1.55	97.43	1.40	153.50	.229
Desaturation index	0.53	1.17	0.09	1.46	145.00	.155
No. of desaturations	4.50	7.75	7.50	13.25	145.00	.155
Delta 12s Index	0.26	0.12	0.34	0.52	112.50	.060
Time below95	0.53	3.47	1.05	3.77	150.50	.455

*Exact significance

7.8.6.1. Effects of nocturnal hypoxia and sleep disturbance on GEF

A general linear model was used to explore hypothesis 5 stated in the introduction – that the presence of nocturnal hypoxia and sleep disturbance will increase a child's susceptibility to neuropsychological deficits. In the model, children were classified as having nocturnal hypoxia if they had either a probable or possible diagnosis using the oximetry parameters (one control child was also included in this group as they had a particularly high score from the CSHQ Sleep-Disordered Breathing subscale). This subset consisted of 23 control children and 17 CF children, four control children were included in the nocturnal hypoxia group (n = 14) and seven children with CF were included in the no hypoxia group (n = 26). The calculations for sleep disturbance and GEF, as described above (section 7.6.3), were re-analysed using the subset of children with oximetry data. As shown in figure 5, a two-way ANOVA revealed a significant main effect of nocturnal hypoxia on GEF scores, $F(1,36) = 4.84$, $p < .05$. There was a non-significant main effect of sleep disturbance, $F(1,36) = 0.18$, $p > .05$. There was no

significant interaction between sleep disturbance and hypoxia on GEF, $F(1,36) = 0.00$, $p > .05$.

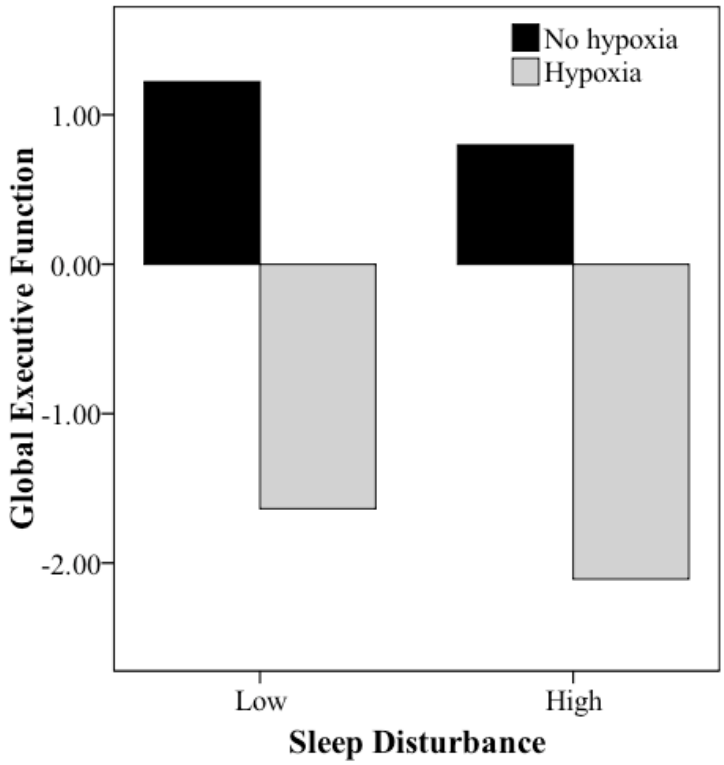

Figure 5 Effects of nocturnal hypoxia and sleep disturbance on GEF

7.8.6.1.1.Effects of nocturnal hypoxia and sleep disturbance on processing speed

As shown in Figure 6, a two-way ANOVA revealed a main effect of sleep disturbance on processing speed that just failed to reach significance, $F(1,36) = 3.31$, $p = .08$. There was a non-significant main effect of hypoxia on processing speed, $F(1,36 = 1.54$, $p > .05$. There was no significant interaction between hypoxia and sleep disturbance on processing speed, $F(1,36) = 0.07$, $p > .05$.

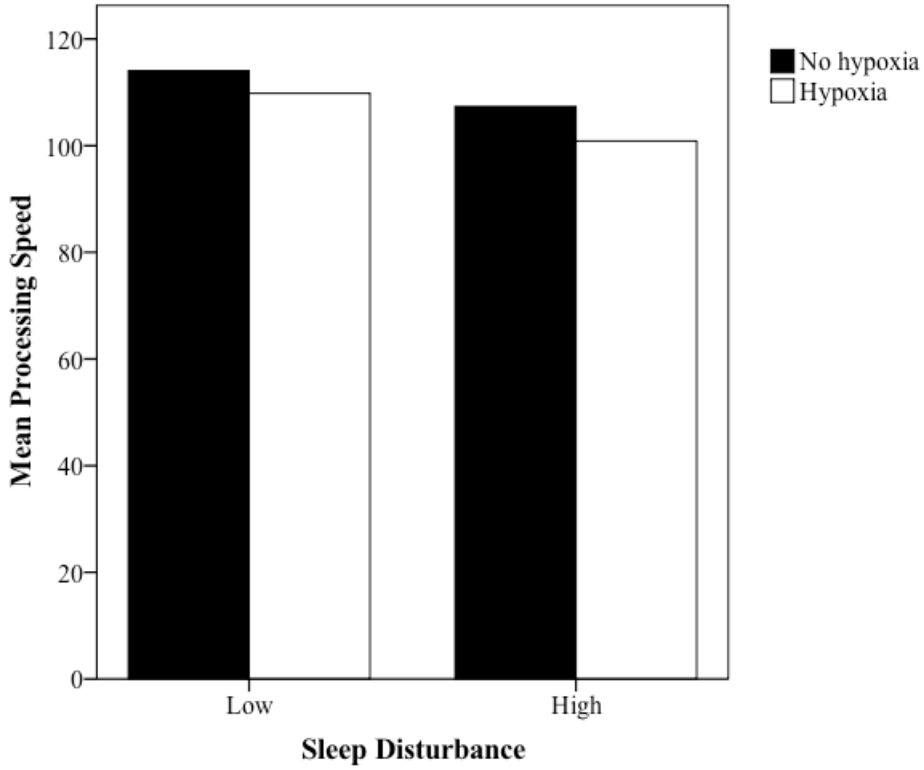

Figure 6 Effects of nocturnal hypoxia and sleep disturbance on processing speed

7.9. Discussion of CF and Control Between-Group Comparisons

The rationale for conducting this study examining sleep and neuropsychological functioning in children with CF was based on previous studies showing increased sleep disturbance in this clinical group. Previous research has also shown that normal healthy children with sleep disturbance have decreased neuropsychological functioning. No previous studies have been conducted examining cognition and behaviour in children with CF. The aim was to determine whether children with CF have increased sleep disturbance compared to the healthy control data collected in Chapter 6, and to determine whether children with CF have deficits in EF that could be attributed to increased sleep disturbance, possibly a consequence of their illness. The study failed to find any significant differences between children with CF and typically developing children with regards to either sleep parameters (both objectively measured actigraphy and parent-reports) or with regards to any measures of EF.

7.9.1. Hypotheses

Hypotheses 3-6 were proposed in the introduction to examine differences between the children with CF and the control sample:

3. Children with CF will have significantly lower sleep duration and sleep efficiency and more wake after sleep onset (the dependent variables), as measured using actigraphy, compared to children without CF (with group – CF or TD as the independent variable).
4. Global executive function will be lower in children with CF compared to controls.
5. There will be a greater incidence of nocturnal hypoxia in children with CF compared to controls.
6. The presence of nocturnal hypoxia and sleep disturbance will increase a child's susceptibility to neuropsychological deficits compared to the presence of sleep disturbance alone.

7.9.1.1. Hypothesis 3

The expectation that children with CF would have increased sleep disturbance compared to controls was based on previous research demonstrating differences in sleep time and sleep quality between CF children and healthy controls. Hypothesis 1 was not

supported as there were no significant differences in actigraphy sleep variables between the two groups.

7.9.1.2. Hypothesis 4

The hypothesis that children with CF would have lower global executive function in EF compared to healthy controls was based on the assumption that children with CF would have increased sleep disturbance as a consequence of their illness. Since the CF group did not have increased sleep disturbance compared to the healthy controls, it is not surprising that they did not have neuropsychological deficits associated with sleep disturbance. The study by Amin et al. (2005) compared actigraphically measured sleep in 44 children with CF and 40 healthy controls aged 8 – 18 years. Compared to controls, sleep efficiency was significantly lower in children with CF and the number of long waking episodes was significantly greater. Sleep duration was also lower in children with CF although it just failed to reach significance (p = .07). This is in contrast to the results of the study reported above, which does not demonstrate any significant differences in sleep parameters between healthy controls and children with CF. Several factors may have contributed to the discrepancies in between previously published results and those presented in this thesis. Of particular importance is the illness severity of the children with CF who participated in this research. In the study by Amin et al. (2005) sleep efficiency was associated with severity of lung disease as measured using FEV (forced expiratory volume). In contrast, all parents of the children who took part in this study noted (anecdotally) that their child/children were quite well and their illness was being well managed. Unfortunately, an independent measure of illness severity was not recorded in this study, although from the parental comments it is likely that most children would have been classified as having either normal or mild lung function. Hence, these children may not have had experienced the nocturnal symptoms that can characterise the disease that disrupt sleep. It is possible that the difference in sleep parameters between children with CF and controls found by Amin et al. (2005) was due to the inclusion of children whose lung disease was severe enough to disrupt the child's sleep. The difference in the age range of this sample (6-13 years) compared to Amin et al. (8-18 years) may also have contributed to the discrepancies. Mean sleep efficiency reported by Amin et al (2005) for control children was high (94.5%) in comparison to the controls in Study 2 (85%). This could be a consequence of the age difference between the two studies, or as a result of different analysis methods. Amin et al. (2005) do not specify which algorithm they use to analyse the raw actigraphy data.

7.9.1.3. Hypothesis 5: hypoxia in children with and without CF

The hypothesis that nocturnal hypoxia would be more frequent in children with CF compared to the healthy controls was partially supported. A comparison of the oximetry data did not reveal any significant differences between the two groups although the delta index was higher in children CF, and just failed to reach significance. This supports the suggestion that the children with CF who participated in this study were quite "well" despite their illness. However a greater proportion of children with CF (59%) were characterised as having a probable or possible diagnosis of hypoxia compared to control children (17%).

7.9.1.4. Hypothesis 6: effects of nocturnal hypoxia and sleep disturbance on executive function and processing speed

The final hypothesis, that nocturnal hypoxia would exacerbate neuropsychological deficits in children with high sleep disturbance was not supported. In the subset of children with oximetry data, only nocturnal hypoxia, and not sleep disturbance, had a significant effect on GEF, which was lower in children classified as having nocturnal hypoxia. This suggests that performance on EF tasks is affected by nocturnal hypoxia irrespective of sleep disturbance. In contrast, high sleep disturbance, but not nocturnal hypoxia, had an effect (albeit not quite significant) on processing speed. Children with high sleep disturbance had lower processing speed compared to children with low sleep disturbance.

7.10. CHAPTER CONCLUSIONS

In summary, this study aimed to determine if children with CF have increased sleep disturbance compared to healthy controls. It was proposed that the nocturnal symptoms experienced by children with CF would put them at greater risk of sleep disturbance compared to healthy controls. The previous study reported in Chapter 6, showed that EF and processing speed was lower in children with high sleep disturbance. Hence it was hypothesised that children with CF would have deficits in EF and processing speed as a consequence of their increased risk of sleep disturbance. However, the results of Study 3 did not emulate the findings of Study 1. When dichotomised into high and low sleep disturbed groups, neither GEF nor processing speed was significantly different between the two groups of children with CF. This is in contrast to Study 1 where both GEF and processing speed was significantly worse in control children with high sleep disturbance.

This study did not find any significant differences in the sleep of children with and without CF. This could explain why no significant differences in EF performance were found between the children with CF and healthy controls. A further aim of the study was to examine whether neuropsychological deficits were greater if the child experienced both high sleep disturbance and nocturnal hypoxia. However, the results indicate that EF deficits were worse in children with nocturnal hypoxia, irrespective of whether they had high or low sleep disturbance. In contrast, processing speed deficits were more evident in children with high sleep disturbance, irrespective of whether they had nocturnal hypoxia.

CHAPTER 8 STUDY 4
A POLYSOMNOGRAPY STUDY OF CHILDREN WITH CF

8.1. INTRODUCTION

Chapter 7 examined sleep disturbance and neuropsychological functioning in a sample of children with cystic fibrosis. The aim of that study was to examine whether children with cystic fibrosis (CF) experience sleep disturbance, possibly as a consequence of nocturnal symptoms such as chronic cough. It was hypothesised that children with CF would have greater sleep disturbance compared to the healthy control sample reported in Chapter 6 (Study 2). It was also hypothesised that children with CF would be at greater risk of the neurocognitive deficits associated with increased sleep disturbance. Study 3 did not find that children with CF were more likely to experience sleep disturbance (as measured using actigraphy), nor did the study find neurocognitive or behavioural deficits in children with CF compared to the healthy control sample.

Although actigraphy is a valid method of characterising sleep patterns, it provides limited information restricted to sleep duration, waking periods, and activity levels but does not provide any information about respiratory function. One of the aims of this thesis was to examine whether the association between neuropsychological dysfunction and sleep disturbance differs in children with SDB compared to children who have no sleep-related breathing problems. Children with CF were selected as a population to study because of previous literature suggesting that they may be at risk of sleep disturbance and nocturnal hypoxia. As noted in earlier chapters, progressive underlying lung disease predisposes patients with CF to hypoxia, which has been associated with sleep disruption in other models of chronic respiratory disease such as obstructive sleep apnoea. In patients with CF, OSA is not the risk factor for hypoxia, but can be caused by hypoventilation, ventilation perfusion mismatch, and hypoxaemia (Hayes, 2006). In addition, upper airway obstruction from nasal polyps may also contribute to the development of hypoxia

As discussed in Chapter 7 few studies have examined sleep in children with CF. Actigraphy studies have shown that children with CF have lower sleep efficiency and more frequent awakenings compared to controls (Amin et al., 2005). A comprehensive search of the literature using Web of Science and Google Scholar found only one

published peer-reviewed paper that has conducted overnight polysomnography in children with CF (Naqvi et al., 2008). Twenty-four children with CF (10-18 years) and 14 control children (6-15 years) underwent one night of full polysomnography. Children and adolescents with CF had significantly lower sleep efficiency compared to control children. The percentage of REM sleep was significantly shorter and REM latency was significantly longer in children with CF. There were no significant differences between the two groups with regards to sleep latency or the percentage of time spent in sleep stages 1,2,3, or 4. Children with CF had significantly lower minimum oxygen saturation and a higher arousal index compared to controls. Severity of lung disease, as measured using FEV (forced expiratory volume), was significantly correlated with sleep efficiency. The results of that study suggest that children with CF have disrupted sleep that may be associated with the severity of their respiratory disease.

In adults with CF, severity of lung disease has been associated with the magnitude of desaturation during sleep. Uyan et al. (2007) suggest that the lack of literature examining sleep and breathing in children could be attributed to the fact that chronic lung dysfunction often does not develop until late childhood. However, studies of very young children with CF have demonstrated nocturnal desaturations in infants with mild airway inflammation (Villa, Pagani, Lucidi, Palamides, & Ronchetti, 2001). Uyan et al. (2007) conducted an overnight study of home pulse oximetry in children with CF who had normal pulmonary function, or mild-moderate lung disease. Nocturnal hypoxia (defined as SpO_2 <90% for >5% for the night) was not found in any patients, however, they did find that 95% of the sample experienced desaturations during sleep. Nocturnal mean SpO_2 was not associated with severity of lung disease (based on FEV) however minimum SpO_2 was significantly lower in children with mid-moderate lung disease compared to children with CF who had normal FEV.

To enable a more comprehensive investigation of the respiratory parameters and sleep architecture of children with CF, a sub-sample of the children with CF who took part in Study 3 underwent overnight full polysomnography. Although PSG provides detailed information of sleep parameters, it does have disadvantages. One night of sleep in the laboratory is unlike to be representative of a child's usual sleep pattern, especially in terms of sleep duration and sleep efficiency as the novel environment is likely to cause some disruption to a child's usual sleep patterns.

8.2. AIMS

The initial aim of Study 4 was to conduct overnight full polysomnography in a subsample of 20 children who participated in Study 3. The initial selection criteria for completing the PSG study was to be based on the actigraphy data – CF children in the top and bottom quartiles of sleep efficiency (as determined using actigraphy) would be asked to participate in the sleep lab study. The main hypotheses to be tested were 1) that high and low sleep disturbance (as determined by actigraphy data from Study 3) is confirmed by polysomnography, and 2) that actigraphic sleep disturbance could be explained by sleep related breathing problems in children with CF.

However, several confounding factors prevented this selection process from occurring. These included significant administrative delays from NHS ethics and R&D, and slow recruitment of CF patients in order to complete Study 3. This resulted in a smaller than planned sample for Study 3, hence from the outset, there were fewer children to select from for the PSG study. Furthermore, an insufficient number of children agreed to take part in the PSG to allow children to be selected, and consequently the children recruited into Study 4 were done so on the basis of whether they agreed to take part. Once these obstacles were overcome, there were additional difficulties involved in recruiting a sleep technician and there were limited nights available to conduct the PSG studies. The combination of these problems resulted in a much smaller than intended sample for Study 4, and the initial aims had to be abandoned because the sample size was not sufficient to conduct the original planned comparisons.

Following these difficulties, the planned data analyses were revised in accordance with the small sample. The data presented here aims to: 1) compare the sleep architecture and respiratory information obtained using PSG with published data on typically developing children and other sample of children with CF, and 2) to compare the data to that obtained in the home in Study 3 using actigraphy and pulse oximetry. If this sample is free from SDB, then the results should be similar to the normative data. If however, the children have lung disease, then they may be more similar to the Naqvi et al sample. It was not anticipated that PSG and actigraphy variables will necessarily be associated – PSG records one night in an artificial environment, often restricting sleep time, whereas actigraphy was recorded for 1 week in the natural environment. However, it may indicate whether the one night of PSG was representative of a usual nights sleep. Given the small sample size for this study, it is acknowledged in advance that any results

should be interpreted with caution. Furthermore, as discussed in Chapter 7, the children with CF who participated in Study 3, were noted by their parents as being well, and that their disease was well managed. However, it was anticipated, given the results published by Naqvi et al. (2007), that sleep efficiency would nonetheless be lower in children with CF compared to normative data. With regards to the respiratory parameters, previous studies have shown that children with CF may have increased desaturations and upper airway obstruction due to nasal polyps. Hence it was hypothesised that children with CF would have lower minimum SpO_2 , lower mean SpO_2 and increased desaturations compared to control data.

Although a thorough testing of associations between the PSG data and the neuropsychological information collected in Study 3 was not possible due to the small sample size, given that previous studies have found behavioural and cognitive difficulties in children with SDB, exploratory analyses were carried out using the aggregated EF scores, and the total scores from the behavioural measures (SDQ and BRIEF) to explore whether they were associated with respiratory or sleep architecture parameters.

8.3. METHOD

8.3.1. Participants

Thirteen of the 26 children with CF who participated in Study 3 agreed to take part in the polysomnography study. Two studies were not completed due to illness on the part of the sleep technician and these could not be rescheduled. Two children could not attend the sleep laboratory on any of the nights that were available. The final number of children who underwent full polysomnography was nine. The children were aged 6 years 2 months to 12 years 10 months (mean age 9 years 3 months). The sample consisted of 4 boys and 5 girls who did not differ with regards to age (t (1,25) = -0.63, df = 25, $p > .05$). There was no difference in the maternal education of families who agreed to take part compared to those who did not (Table 29).

Table 29 Maternal education of children who did and did not take part in the PSG study

	Non-participants	Participants
No qualifications	3 (12%)	3 (12%)
GCSE/O Levels	5 (19%)	5 (19%)
A levels/NVQ/Highers	38 (44%)	5 (19%)
Degree	2 (8%)	2 (8%)
Postgraduate degree	3 (3%)	5 (19%)
Missing	3 (11%)	6 (23%)

Severity of lung disease in the CF patients was not assessed at the time of the PSG. However, clinical information regarding lung function at the last check-up was obtained from medical records for eight of the nine children and is shown in Table 30. FEV1% is a measurement of the amount of air that the child can forcibly blow out in one second, expressed as a percentage, and is one of the primary indicators of lung function. Four children had normal FEV1% (> 90% predicted), two children had mild degree of lung disease (70-89% predicted) and two children had moderate (40-69% predicted) lung disease. Chest XR is a longitudinal assessment of chest x-ray and measures severity of lung changes on a score of 0-20, where 20 represents the worst score.

Table 30 Clinical information regarding severity of lung disease in children with CF

	FEV1% predicted	Chest XR score	ENT problems
P1	62.9	5	Allergic rhinitis
P2	92	2	None
P3	81.5	1	None
P4	n/a	n/a	n/a
P5	104	5	None
P6	68	N/A	Nasal polyps
P7	96	5	Seasonal allergic rhinitis
P8	98.5	4	None
P9	86	N/A	None

8.3.2. Polysomnography

The following parameters were recorded simultaneously: bilateral electroocculogram (EOG), electroencephalogram (EEG; C3A2, O1A2, C4A1, O2A1), chin electromyogram (EMG), anterior tibialis EMG, tracheal microphone, electrocardiogram (ECG), diagphramatic EMG, thoracic and abdominal excursions (piezo technology), nasal airflow (Protech, Mukilteo, WA), finger pulse oximetry (Masimo technology). All measures were digitised using a commercially available polysomnography system (Alice 5 sleepware systems Respironics UK Ltd, Chichester West Sussex) and a digital time-synchronised video recording was performed. Sleep staging was scored using standard criteria (Rechtschaffen & Kales, 1968) by the attending sleep technician. Respiratory arousals were defined as changes in EEG frequency of ≥ 3 second after an apnoea or hypopnoea and only scored in REM if accompanied by an increase in submental EMG amplitude. A minimum of 10 seconds of intervening sleep was necessary to score a second arousal. Obstructive apnoea was defined as the presence of chest/abdominal wall movement in the absence or decrease of airflow by >80% of the preceding breath for ≥ 2 breaths. Hypopnoeas were classified as for apnoeas but where the reduction in flow was 50%-80% of the previous breath. The apnoea/hypopnoea index (AHI) was defined as the number of obstructive apnoeas, hypopnoeas, and mixed apnoeas per hour of total sleep time. Central apnoeas were identified from the respiratory inductance plethysmography. Sleep efficiency was defined as the percent of time scored as sleep during the time in bed.

8.3.3. Procedure

Ethical approval was initially obtained from the Ethics Committee in the School of Psychology, University of Southampton. NHS ethical approval was obtained from the Isle of Wight, Portsmouth, and South West Hampshire Local NHS Ethics Committee (REC reference number 08/HO51/2008, see Appendix C.1). NHS R&D approval was obtained from Southampton General Hospital. Details of the overnight sleep laboratory study were first explained to parents during the initial telephone contact for Study 3. It was emphasised to parents that participation in Study 3 did not obligate families to undergo the overnight sleep study. Further details of the polysomnography were given to families during the first visit of Study 3 (Appendix D.1). In all but one case, the polysomnography was carried out after the actigraphy in Study 3. In one case, due to

time constraints, the child attended for polysomnography prior to completing the actigraphy part of Study 3.

All children were free of acute respiratory exacerbation or other acute illness at the time of the study. Families were instructed to arrive at the laboratory approximately 1 hour before bedtime, usually between 7:30pm and 9:00pm. Written consent was obtained from parents and children (Appendix D.2). Children were studied for up to 12 hours in a quiet dark room and in the company of their parents. Studies were terminated between 6:00am and 7:00am the next morning. Some children woke up naturally within this time, and others had to be woken by the sleep technician.

8.3.4. Statistical Analyses

The following sleep variables were evaluated:

- Total sleep time (TST): REM + NREM + movement (during SPT)
- Sleep period time (SPT)
- Sleep efficiency (calculated as 100 x TST)
- Time in bed (TIB): calculated as the time from lights off to lights on
- Sleep latency: time to first 2 minutes of continuous stage 2 sleep
- Wake during sleep: SPT – TST
- REM latency: calculated as the number from minutes from sleep onset to the first REM sleep cycle
- Percentage of (and minutes) sleep stages (in TST) 1,2, ¾ (SWS), and REM
- Hypopnoea index
- Obstructive apnoea index
- Apnoea-hypopnoea index (AHI): Obstructive apnoea index + mixed apnoea index + hypopnoea index
- Mean SpO_2
- Minimum SpO_2 (SpO_2 nadir)

Due to a lack of a control sample for this study, published data of polysomnography normal values of sleep architecture and respiratory values were used to compare the data obtained in this study with that of typically developing children. There is limited published data of normal reference values for PSG in children, however a recent study of European children aged 6-16 years was considered appropriate as the age range of the group is most similar to the 9 participants in this study (Verhulst et al., 2007). In addition, the PSG results were also compared to the only published data of PSG values

in children with CF (Naqvi et al., 2008). One sample t tests were used throughout to compare the data obtained in this study with that of previous studies. Associations between PSG values and the neuropsychological results obtained in Study 3 (Chapter 3) were explored using Pearson correlation co-efficients.

8.4. RESULTS

8.4.1. Polysomnography

8.4.1.1. Sleep architecture compared to controls

Table 31 shows the raw PSG data for each child. Table 32 shows the mean, *SD*, and range of the PSG sleep architecture variables for the nine children with CF. Also presented in this table are the means, *SD*, and range (where published) from Verhulst et al. (2007) of non-snoring children. A one-sample t test showed that the mean total sleep time of children with CF was significantly shorter to the data reported by Verhulst et al. (2007), $t(1,8) = -2.94$, $p = .019$. Sleep efficiency was not significantly different between the two groups, but sleep latency was significantly shorter in the children with CF compared to the normative values published by Verhulst et al. (2007), $t(1,8) = -2.62$, $p = .031$. The percentage of TST spent in stage 1, stage 2, and slow wave sleep was not significantly different between the two groups, however, the percentage of TST spent in REM sleep was significantly greater in children with CF, $t(1,8) = -5.99$, $p < .001$. Children with CF also had longer REM latency times although this just failed to reach significance $t(1,8) = 2.28$, $p = .52$. There was no significant difference in arousal index or sleep efficiency between the two groups.

Table 31 Raw PSG data for children with CF

	P1	P2	P3	P4	P5	P6	P7	P8	P9
Age	123.0	76.0	121.0	100.0	145.0	154.0	150.0	132.0	107.0
Gender	F	F	M	F	F	F	M	M	M
TST	444.0	410.5	446.5	242.5	435.5	434.5	388.5	335.5	458.0
SE	89.0	77.7	87.4	64.8	90.7	94.5	74.0	71.5	86.7
TIB	496.0	528.0	511.0	374.0	480.0	460.0	522.0	469.0	5278.0
SL	52.0	40.0	61.0	6.0	29.5	6.5	32.0	11.5	13.5
Wake	0.00	77.5	3.5	18.5	15.0	19.0	101.0	122.0	37.0
SPT	444.0	488.0	450.0	261.0	450.5	453.5	490.0	457.5	495.0
S1%	0.0	0.6	0.3	1.9	2.6	2.4	1.2	3.6	0.3
S2%	40.8	33.1	32.9	41.0	66.7	50.3	33.3	48.1	43.3
SWS%	44.6	48.6	53.6	38.6	23.7	26.7	45.2	41.0	4.9
S1 min	1.0	4.0	4.0	8.0	14.0	13.5	6.5	13.5	7.0
S2 min	181.0	136.0	147.0	99.5	290.5	218.5	129.5	161.5	198.5
SWS min	198.0	199.5	239.5	93.5	105.0	116.0	176.0	137.5	205.0
REM%	14.4	16.4	12.2	18.1	4.8	16.6	18.9	6.6	11.4
REM min	64.0	67.5	54.5	44.0	21.0	72.0	73.5	22.0	52.0
REM cycles	3	4	2	2	2	6	2	3	2
REM lat	136.0	124.5	243.5	73.0	207.5	111.5	351.0	163.0	355.0
Mean SpO_2	94.0	98.0	97.0	95.2	98.9	95.8	96.0	96.0	94.9
SpO_2 nadir	85.0	97.0	83.0	93.0	96.0	91.0	94.0	94.0	66.0
HI	0.0	0.0	0.5	0.0	1.1	0.0	0.0	0.0	0.0
OAI	1.6	0.1	0.3	0.0	1.2	0.1	0.2	0.4	0.5
AHI	1.9	0.7	1.1	0.7	3.0	0.2	0.5	0.4	0.6

(TST = total sleep time; SE = sleep efficiency; TIB = time in bed; SL = sleep latency; Wake = wake after sleep onset; SPT = sleep percent time; S1% = percent of TST in stage 1; S2% = percent of TST in stage 2 sleep; SWS% = percent of TST in slow wave sleep; S1 = number of minutes in stage 1; S2 = number of minutes in stage 2; REM% = percent of TST in REM; REM min = number of minutes in REM sleep; REM lat = REM sleep latency; HI = hypopnoea index; OAI = obstructive apnoea index; AHI = apnoea hypopnoea index)

Table 32 Comparison of PSG sleep architecture of children with CF to control data (Verhulst et al., 2007) and children with CF (Naqvi et al.,2007)

	CF (n = 9)			Verhulst et al.			t test (df = 8)		Naqvi et al.		t test (df = 8)	
	Mean	*SD*	Range	Mean	*SD*	Range	*t*	*p*	Mean	*SD*	*t*	*p*
Total sleep time	399.50	69.92	242 – 458	468	48	-	-2.94	.019	-	-	-	-
Sleep efficiency	81.73	10.17	64 – 94	80.5	8.5	-	0.36	.725	75.2	2.5	1.93	.090
Sleep latency	28.00	20.17	6 – 61	45.6	29.4	-	-2.62	.031	36.9	5.9	-1.32	.222
Wake during sleep	49.19	44.80	4 – 122	-	-	-	-	-	-	-	-	-
Sleep period time	443.28	71.14	261- 495	-	-	-	-	-	-	-	-	-
Stage 1 (mins)	7.94	4.75	1 – 14	-	-	-	-	-	-	-	-	-
Stage 2 (mins)	173.56	57.07	99-290	-	-	-	-	-	-	-	-	-
SWS (mins)	163.33	51.71	93 – 234	-	-	-	-	-	-	-	-	-
REM minutes	52.28	19.93	21-74	-	-	-	-	-	-	-	-	-
REM latency	196.11	102.33	73 – 355	118.4	49.9	-	2.28	.052	150.5	16.6	1.34	.218
Stage 1 % TST	1.43	1.25	0 – 3	2.3	2	0.1-13	-2.07	.072	12.1	1.4	-25.52	.000
Stage 2 % TST	43.28	10.86	32 – 66	42.5	7.2	22-65	0.22	.835	49.7	1.6	-1.77	.114
SWS % TST	36.32	15.26	4 – 53	32	-	10-62	0.85	.420	25.1	-	2.21	.058
REM %TST	13.27	4.98	4 – 19	23.2	4.9	-	-5.99	.000	12.7	1.5	0.34	.741
Arousal index	7.49	3.88	1-13	6.2	1.8	-	0.98	.348	28.3	2.9	-16.09	.000
Mean SpO2	96.1	1.66	94-99	97	0.6	96-98	-1.63	.142	-	-	-	-
Min SpO2	88.78	9.77	66-97	91.5	3	82-96	-0.84	.427	90.3	1.1	-0.47	.653
Hypopnoea index	0.18	0.38	0-1.1	1.10	0.87	-	-7.22	.000	-	-	-	-
Obstructive apnoea index	0.49	0.55	0-1.6	0.33	0.26	0-0.87	0.87	.410	-	-	-	-
Apnoea hypopnoea index	1.01	0.90	0.2-3	0.33	0.26	0-0.87	2.28	.052	-	-	-	-

8.4.1.2. Sleep architecture compared to Naqvi et al. (2007)

As shown in Table 32, sleep efficiency of the children with CF was higher than the data reported by Naqvi et al. (2007) in children aged 8-18 with cystic fibrosis, although this did not reach significance, $t(1,8) = 1.93$, $p = .09$. Sleep latency did not differ between the two groups, nor did the percentage of REM sleep, or REM sleep latency. A significant difference was found in the percentage of stage 1 sleep – the results reported by Naqvi et al (2007) were much higher than the data found for this study, $t(1,8) = -25.52$, $p < .001$. REM sleep was not significantly different between the two groups, however, the arousal index reported by Naqvi et al. (2007) was significantly greater than the arousal index of this sample of children with CF.

8.4.1.3. Respiratory results compared to controls

Table 31 reports the raw respiratory values for each child and Table 32 shows the mean, SD, and range of respiratory values for the children with CF, as well as the data published by Verhulst et al. (2007) of non-snoring children. Compared to non-snoring children, the apnoea-hypopnoea index was higher in this sample of children with CF, although this just failed to reach significance, $t(1,8) = 2.28$, $p = .052$. In contrast, the hypopnoea index in this sample of children with CF was significantly lower compared to the control data, $t(1,8) = -7.22$, $p < .001$. This result suggests that the high AHI in this sample of children with CF is a consequence of a high number of obstructive and mixed apnoeas. The only respiratory variable that was reported by Naqvi et al. (2007) was minimum SpO2. The one-sample t test showed no significant difference between the two groups.

8.4.2. Associations Between Sleep Laboratory and Home Monitoring Data

8.4.2.1. Comparison of polysomnography and actigraphy

Correlations between the data obtained from one night of PSG and the data obtained from one week of actigraphy are shown in Table 33. As shown in figure 7, sleep latency, as measured using actigraphy, was significantly associated with time in bed as measured using PSG, r = -.75, p = .019. When this correlation was recalculated, excluding the outlying data point, the correlation was no longer significant, r = -.16, p = .714. No other significant associations were found between the two measures.

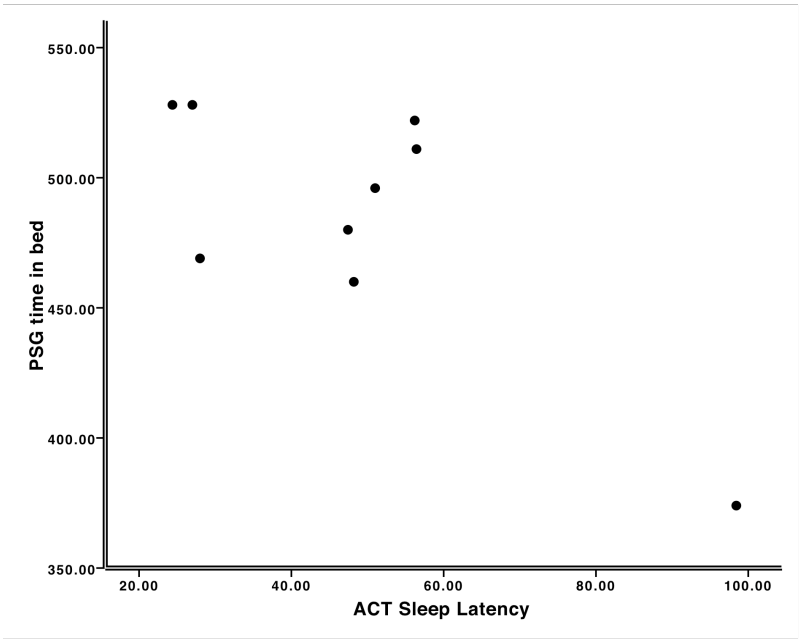

Figure 7 Association between PSG time in bed and ACT sleep latency

Table 33 Pearson correlation coefficients of polysomnography (PSG) and actigraphy (ACT) in CF children (n = 25)

	1	2	3	4	5	6	7	8	9	10
PSG sleep efficiency	1.00									
PSG sleep latency	0.29	1.00								
PSG total sleep time	**0.88**	0.50	1.00							
PSG time in bed	0.41	0.56	**0.79**	1.00						
PSG wake after sleep onset	-0.58	-0.26	-0.30	0.23	1.00					
ACT sleep duration	-0.56	0.06	-0.27	0.15	0.33	1.00				
ACT sleep minutes	-0.36	-0.24	-0.21	0.02	0.15	0.63	1.00			
ACT sleep efficiency	-0.08	-0.33	-0.08	-0.07	-0.03	0.13	**0.86**	1.00		
ACT sleep latency	-0.35	-0.10	-0.61	**-0.75**	-0.43	-0.17	-0.02	0.07	1.00	
ACT wake after sleep onset	0.00	0.34	0.04	0.09	0.08	0.01	**-0.77**	**-0.99**	-0.10	1.00

Significant correlations, $p < .05$, shown in bold script

Table 34 Pearson correlation co-efficients of PSG and home pulse oximetry data

	1	2	3	4	5	6	7	8	9	10	11
PSG											
Apnoea hypopnoea index	1.00										
Hypopnoea index	**.81**	1.00									
Obstructive apnoea index	**.81**	.41	1.00								
SpO_2 nadir	.15	.20	-.12	1.00							
SpO_2 mean	.27	.60	-.23	.66	1.00						
Home											
SpO_2 nadir	.30	.24	.03	**.95**	.58	1.00					
SpO_2 mean	.35	.31	.13	**.89**	.54	**.83**	1.00				
Number of desaturations	-.20	-.18	-.01	**-.92**	-.45	**-.86**	**-.96**	1.00			
Desaturation 4% index	-.19	-.16	-.01	**-.93**	-.45	**-.87**	**-.96**	**1.00**	1.00		
Time spent <95%	-.38	-.20	-.27	-.15	-.21	-.24	**-.77**	.01	-.02	1.00	
Delta index	-.23	-.06	-.49	-.34	.09	-.42	-.06	.56	.59	-.25	1.00

Significant correlations, $p < .05$, shown in bold script

8.4.2.2. Comparison of home and PSG pulse oximetry

As shown in Table 34, PSG measured SpO_2 nadir was significantly correlated with the home recorded SpO_2 nadir, $r = .95$, $p < .001$ (see figure 8) and also home recorded mean SpO_2, $r = .89$, $p = .001$. PSG SpO_2 nadir was also significantly correlated with the home measured number of desaturations, $r = .92$, $p < .001$, and the desaturations below 4% index, $r = .93$, $p < .001$.

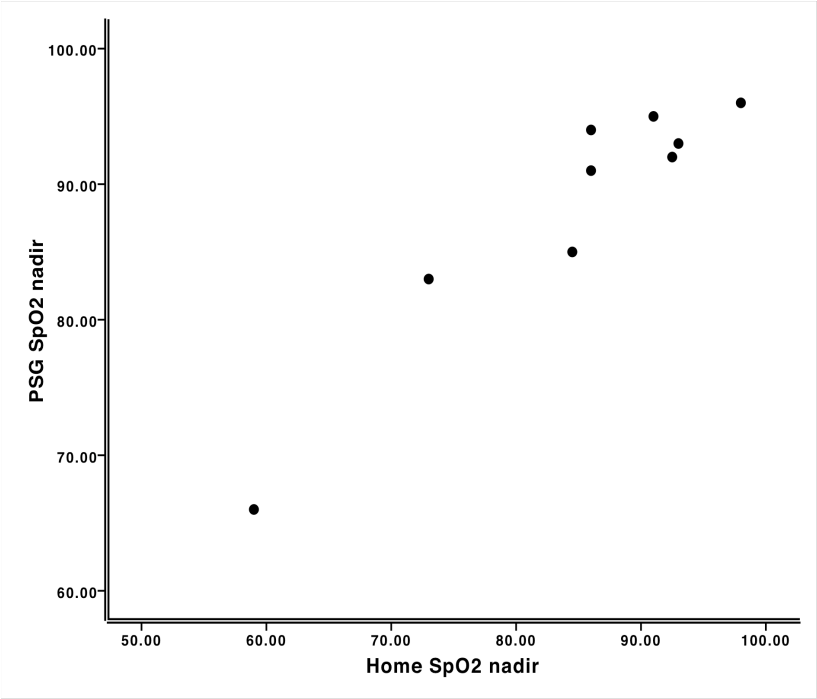

Figure 8 Scatterplot showing positive relationship between PSG and home measured SpO_2

Table 35 Pearson correlation co-efficients of PSG variables, processing speed, and global executive function

	1	2	3	4	5	6	7	8	9	10	11	12
Sleep efficiency	1.00											
Sleep latency	.29	1.00										
Total sleep time	**.88**	.50	1.00									
% of TST in stage 1	-.24	-.65	-.47	1.00								
% of TST in stage 2	.38	-.41	.09	.64	1.00							
% of TST in slow wave sleep	-.36	.60	-.24	-.14	-.57	1.00						
Apnoea hypopnoea index	.40	.43	.31	-.05	.56	-.07	1.00					
SpO_2 nadir	-.34	-.05	-.45	.59	.21	.53	.15	1.00				
Processing Speed	.24	-.35	.13	.26	.56	-.56	.24	.05	1.00			
GEF	.17	.16	.40	.22	.30	-.04	.25	.16	.28	1.00		
Total SDQ	.29	.17	.10	-.06	.50	-.18	**.80**	.20	.59	-.04	1.00	
Total BRIEF	.41	.31	.25	-.02	.57	-.10	**.91**	.28	.46	.11	**.94**	1.00

Significant correlations, $p < .05$, shown in bold script

(TST = total sleep time,;GEF = global executive function)

8.4.3. PSG and Neuropsychological Data

Exploratory analyses are presented examining associations between the aggregated cognitive and behavioural data collected in Study 3.

8.4.3.1. Executive function and processing speed

As shown in Table 35, neither Processing Speed nor Global Executive Function were significantly associated with any PSG variables.

8.4.3.2. SDQ & BRIEF

As shown in Table 35, the apnoea-hypopnoea index was significantly correlated with the total SDQ score (r = .80, p = .01) and the total BRIEF score (r = .91, p = .001). An inspection of the scatter plots shown in figures 9 and 10, indicates that those associations were affected by outliers. When the outlying data point was excluded from the data analyses, the association between AHI and total SDQ was still in the expected direction although no longer significant. (r = .445, p = .269). Likewise, the correlation between AHI and total BRIEF was also reduced when the outlier was excluded, although this just fails to reach significance (r = .683, p = .062)

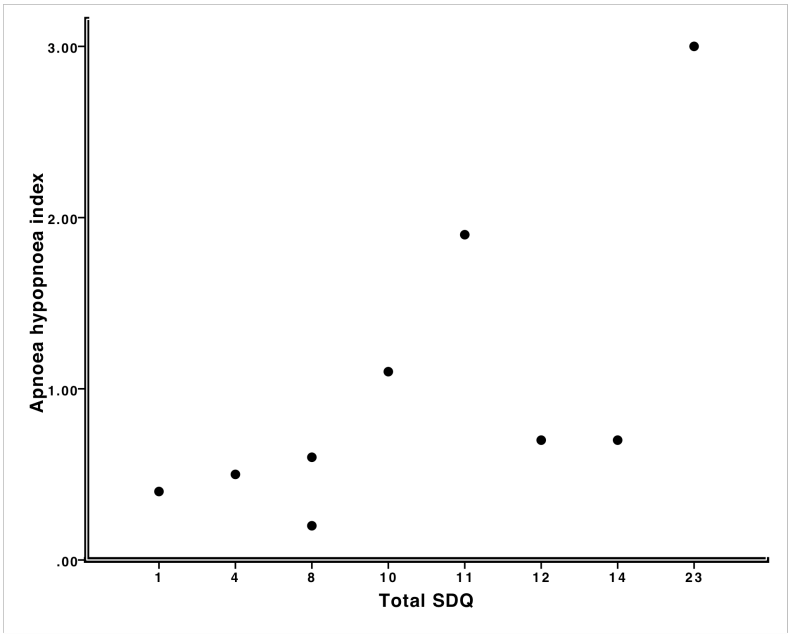

Figure 9 Scatterplot showing relationship between apnoea-hypopnoea index and total SDQ

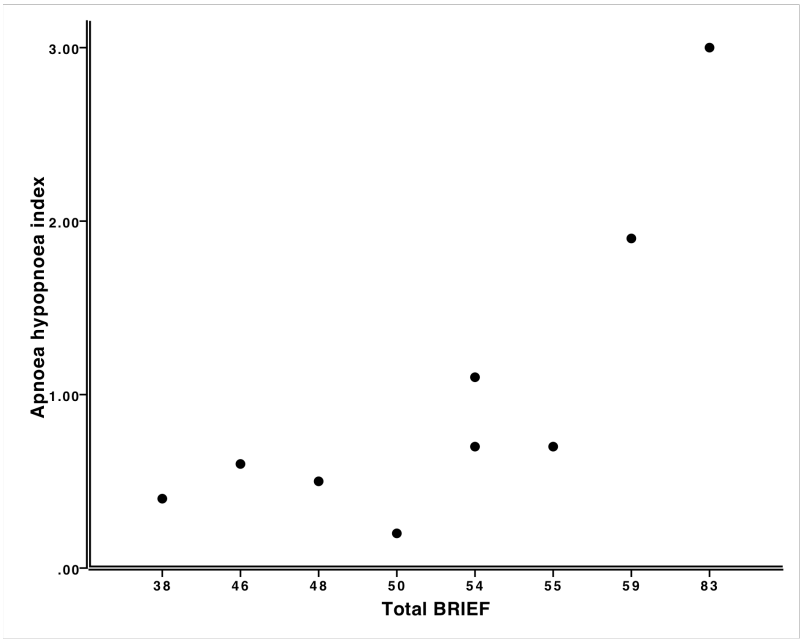

Figure 10 Scatterplot showing relationship between apnoea hypopnoea index and total BRIEF scores

8.5. DISCUSSION

The aim of Study 4 was to obtain detailed information regarding the sleep architecture of children with CF and to compare this with the actigraphic and pulse oximetry data obtained in the home. These data are currently lacking in the literature, and to the best of my knowledge only one peer-reviewed paper has been published that has examined PSG measured sleep architecture in children with CF. The data obtained in this study must be treated with caution due to the small sample size. Furthermore, the clinical data presented in Table 31 shows that six of the children who participated in this study had normal to mild severe lung disease, and two children had moderately severe lung disease. This is in contrast to previous studies of sleep in children with CF (Naqvi et al., 2007) whose sample included five children with moderately severe lung disease and 11 children with severe lung disease.

8.5.1.1. Comparison of sleep architecture results to previous literature

The results of this study suggest that children with CF have shorter sleep times when compared to typically developing healthy children. TST as measured using PSG was significantly shorter when compared to the data published by Verhulst et al. (2007). However, this is not unexpected given that sleep time in the laboratory is unlikely to be representative of a child's usual sleep time. It is not clear from the study by Verhulst et al. (2007) whether children were woken in the morning or allowed to wake naturally. In this study, some children were woken in the morning, hence they may not have had as much sleep as they have usually done so. TST was not reported by Naqvi et al. (2007) so it is not possible to assess whether the TST data in this study are a true reflection of children with CF. Sleep latency was also significantly different when compared to the normative data. Children with CF took less time to fall asleep when compared to typically developing children. When compared to the data published by Naqvi et al. (2007) also examining children with CF, there was no significant difference, suggesting that the sleep latency times collected in this study are indicative of children with CF. Sleep efficiency in children with CF was not significantly different when compared to either the normative data nor the previous CF data. In contrast, Naqvi et al. (2007) found that sleep efficiency was significantly different to controls. Although sleep efficiency was not significantly different to normative data in this sample, it was higher than the mean reported by Naqvi et al. (2007) but failed to reach significance. One

explanation for the lack of a difference between the CF sample and the controls, is that the sleep efficiency reported by Verhulst et al. (2007) is quite low (81% compared to 85% in the controls reported by Naqvi et al. 2007). Another possible explanation is that Naqvi et al. (2007) reported that sleep efficiency was significantly correlated with disease severity – if greater lung disease leads to greater sleep disturbance (as measured using sleep efficiency), children with less severe lung disease will have less sleep disturbance, and hence higher sleep efficiency. In this study, as already noted above, most children had normal or mild lung disease and many parents also reported that their child's disease was well managed and that the child was not particularly unwell at the time of the study.

Children with CF spent a similar percentage of their TST in SWS when compared to normative data, although when compared to the previously published data on children with CF they spent longer in SWS, although this just failed to reach significance. Children with CF had a longer REM onset latency compared to normative data, although this just failed to reach significance, and could be a consequence of the outlier. REM latencies were not significantly different when compared to the data of Naqvi et al. (2007). The percentage of TST spent in REM sleep was significantly shorter in the children with CF when compared to normative data, however when compared to previous CF data (Naqvi et al., 2007) there was no difference. Naqvi et al. (2007) found that children with CF spent a greater proportion of their time in REM sleep compared to controls. These data suggest that children with CF spend longer in REM sleep compared to children without CF.

8.5.1.2. Comparison of respiratory data to normative data

The respiratory data obtained in this study did not show many differences between children with CF and the normative data published by Verhulst et al. (2007). The only significant difference was the hypopnoea index, which was lower compared to normative data. However, the apnoea-hypopnoea index was higher in children with CF, although this just failed to reach significance. This difference is most likely due to the increased number of obstructive apnoeas in the children with CF. Of note is that three children had an apnea-hypopnea index of >1, which is considered abnormal.

8.5.1.3. Comparison of PSG and actigraphy

Pearson correlation co-efficients were used to compare the sleep data from PSG and actigraphy. The only significant association was a negative between time in bed as measured using PSG and sleep latency as measured using actigraphy. An inspection of the scatterplot shown in figure 9 suggests that an outlier skews this association. No other significant correlations were found, which could suggest that little agreement exists between the two methods of sleep measurement. However, the small sample size negates the possibility that the results can be considered truly representative. Furthermore, the two measurements were taken at different time points, and in some cases the actigraphy was conducted several weeks before the PSG. Also both have inherent limitations – actigraphic sleep latency is dependent on parental report and PSG total sleep time is influenced by external factors e.g. the sleep technician waking child in morning.

8.5.1.4. Comparison of home and PSG oximetry

Home and pulse oximetry was measured using the same technology (Masimo) so it is therefore not surprising that the two measures were highly correlated. Nonetheless, as they were taken at different time points, it is reassuring that they were associated. Both SpO_2 nadir measurements were highly correlated. Mean SpO_2 was not significantly associated, although the correlation was strong the lack of a significant result could be due to the small sample size.

8.5.1.5. PSG and neuropsychological results

Due to the small sample size it was not considered appropriate to conduct multiple tests examining associations between the PSG data and the numerous cognitive and behavioural data from Study 3. Instead, a more general overview of the PSG and neuropsychological data was deemed appropriate. Hence, the GEF score used an aggregated measure of EF was used to assess any relationship between PSG variables and cognition, and the total scores from the SDQ and the BRIEF were used to assess relationships between PSG variables and behaviour, rather than the numerous subscales. None of the sleep architecture variables were associated with the GEF, processing speed, SDQ, or BRIEF. From the respiratory variables, the apnoea-hypopnoea index was significantly correlated with both the total SDQ and the total BRIEF scores, however the scatterplots showed that an outlier was influencing these associations.

When the analyses were recalculated, excluding the outlying data point, both correlations were high, albeit no longer significant.

8.5.1.6. Limitations

As already noted, this study was limited by a very small sample size. Several factors contributed to this outcome. The participants for Study 4 were drawn from the pool of participants in Study 3, which itself had fewer participants than originally planned. Of the children who participated in Study 3, only thirteen children agreed to undertake the PSG and unfortunately four of these children could not be tested because there was limited access to the sleep laboratory and no mutually convenient times were available and also because the sleep technician was unwell and these appointments could not be rescheduled. The lack of a control groups is another limitation of this study. Although one sample t tests were conducted using previously published data of healthy children, a suitable control group would have enhanced the methodology of the study. Measuring severity of lung disease using FEV at the time of the PSG would also have improved the study design.

8.5.2. Chapter Conclusions

The results of this study suggest that sleep architecture and respiratory function in children with CF and normal to mild/moderate lung disease does not differ significantly from the sleep architecture of typically developing healthy children. Furthermore, the results do not show any relationship between neuropsychological performance and sleep architecture. However, the small sample size and lack of control group are major limitations that prevent generalising these results to the population of children with CF.

CHAPTER 9
GENERAL DISCUSSION

9.1. Summary of Thesis Aims and Findings

This thesis examined the relationship between sleep and neuropsychological functioning in healthy, typically developing children and in children with cystic fibrosis. The rationale for this thesis came from the theory that one function of the human sleep process is to enable the frontal cortex to rest and recover. Sleep disturbance, therefore, may lead to poor functioning of the frontal cortex and neuropsychological functions associated with that part of the brain (Beebe & Gozal, 2002; Horne, 1988). This is an under-researched area, particularly with children, where research has only recently begun to understand the full impact of sleep disturbance on the developing brain. Although research has begun to examine the association between sleep and neuropsychological functioning in children, the majority of studies have examined this relationship in the context of SDB problems, rather than healthy children who may have sleep disturbance in the absence of any respiratory problems. Those studies that have used healthy samples have often examined only one or two areas of cognitive or behavioural functioning. Therefore an aim of this thesis was to extend knowledge by investigating a range of cognitive abilities deemed to reflect 'executive function' as well as behavioural manifestations of executive function and behaviour problems in general. Furthermore, the thesis aimed to examine whether sleep disturbance, in the absence of sleep disordered breathing, affects neuropsychological functioning in a comparable way to sleep disturbance associated with hypoxia by examining a population of children (cystic fibrosis) deemed to be at risk of hypoxia due to pathology of the respiratory tract.

The studies reported in this thesis found that increased sleep disturbance is associated with poorer global executive functioning and processing speed in healthy, typically developing children. A similar pattern of results was found for children with CF, although in this case not all the results were statistically significant. In healthy, typically developing children, sleep quantity was a better predictor of EF than sleep quality. Nocturnal hypoxia also had a significant effect on global executive function. Sleep disturbance was consistently associated with increased parental reports of conduct problems.

This Chapter provides a summary of the findings of the four empirical studies that were conducted followed by a discussion of how the findings relate to the thesis aims and also how they relate to previous research findings. The implications of these findings, the limitations of the research, and suggestions for future research are also discussed.

9.2. Summary of Key Findings From Studies 1-4

9.2.1. Study 1: Sleep Disturbance and Neuropsychological Functioning in Children

9.2.1.1. Executive function findings

Study 1 aimed to examine behaviour and EF in healthy, typically developing children aged 6-11 years. The rationale behind Study 1 was the findings of Steenari et al. (2003) who found better working memory performance was associated with higher sleep efficiency and shorter sleep latency in healthy children aged 6-13 years. Study 1 aimed to extend the findings of Steenari et al. (2003) by including additional measures of EF, particularly attention, which was not measured by Steenari et al. (2003). The n-back task used by Steenari et al. (2003) relies heavily upon attentional processes; hence it could be argued that an attentional deficit was responsible for their results. Study 1 did not find a significant association between working memory and sleep efficiency or sleep latency and this may have been a consequence of the differing measures used to assess working memory. No other significant associations were found between the actigraphic sleep variables and the EF variables. However, using an aggregate measure of EF performance, children with increased sleep disturbance (as measured using an aggregate of sleep efficiency, sleep latency, and activity level) had significantly worse aggregated EF scores. This finding adds some support to the theory that EF is impaired by sleep disturbance.

9.2.1.2. Behavioural results

In contrast to previous research (Sadeh et al., 2002), Study 1 did not find that increased sleep disturbance, as measured using actigraphy, was associated with increased rates of behaviour problems as rated by parents using the SDQ. Measures of behavioural manifestations of executive dysfunction using the BRIEF were also not associated with any actigraphy sleep measures. However, parental reports of sleep problems, as

measured using the CSHQ, were associated with higher rates of Conduct Problems and hyperactivity. Likewise, parental reports of sleep problems were also associated with increased problems as reported using the BRIEF.

9.2.2. Study 2: Sleep Disturbance and Neuropsychological Functioning in Children II

9.2.2.1. Executive function findings

Study 1 used the CANTAB to measure EF, however it was noted that some children appeared impatient to complete the tasks and/or did not totally understand the task procedures. As a consequence of these methodological concerns, Study 2 began with an extensive revision of the battery of tests to be used for the forthcoming studies. The model proposed by Beebe & Gozal (2002) was used as a basis for determining a new battery of neuropsychological tests. In addition, Study 2 introduced pulse oximetry technology to measure nocturnal symptoms of hypoxia. As in Study 1, Study 2 did not find that working memory performance was associated with sleep efficiency, in contrast to Steenari et al (2003). However, better working memory performance (as measured using the NEPSY tower task and a Backward Digit Recall task) was associated with longer sleep minutes. Study 2 also introduced a measure of processing speed, since there was recent evidence that it may be affected by sleep disturbance (Hill et al., 2006). The results demonstrated that faster processing speed was significantly associated with longer sleep duration. However, the majority of the EF tasks were not associated with actigraphic sleep variables (such as less sleep time or lower sleep efficiency). Nonetheless, in line with Study 1, when performance on the EF tasks was aggregated, children with greater sleep disturbance characterised by lower sleep efficiency and less sleep minutes) had significantly worse executive functioning than children who were classified as having less sleep disturbance. Children with high sleep disturbance also had significantly lower processing speed.

Study 2 also examined the relative importance of sleep quality (as measured using sleep efficiency) and sleep quantity (actual sleep minutes) on neuropsychological functioning. Both sleep quality and sleep quantity were significant predictors of global executive function but sleep quantity explained an additional unique proportion of the variance. Measures of non-executive function were also included in Study 2 to ensure that any cognitive deficit was specific to EF and did not generalise to simple memory tasks.

Simple digit span was not associated with any sleep variables supporting the notion that sleep disturbance has a specific effect on EF and not cognitive functioning in general.

The findings of studies one and two highlight important notions regarding the nature of the EF deficit associated with sleep disturbance. The findings of these two studies support the existence of an *overall* executive function deficit associated with increased sleep disturbance. Discrete tasks that measure individual executive functions may not be sensitive enough to identify statistically significant specific deficits. It is possible that sleep disturbance may have a subtle effect on EF by suppressing the performance of several cognitive processes. Therefore, if researchers attempt to examine EF processes in isolation, they may not observe any statistically significant differences. Indeed, if sleep disturbance has a detrimental effect on EF via the prefrontal cortex, then one would expect the dysfunction to be global, affecting all processes that are subserved by the prefrontal cortex rather than specific to only one cognitive process.

9.2.2.2. Behaviour findings

Study 2 found an association between conduct problems and sleep problems. Increased parental reports of conduct problems were consistently associated with actigraphy sleep variables (less sleep time, lower sleep efficiency, and longer sleep latency). Furthermore, sleep latency was significantly correlated with almost all the SDQ sub-scales. When sleep disturbance was dichotomised, children in the high sleep disturbance group had significantly greater conduct problems compared to children in the low sleep disturbance group. Measures of behaviour problems using the BRIEF were also significantly associated with some actigraphic sleep variables. In particular, sleep duration was significantly associated with most subscales of the BRIEF, including working memory. These findings demonstrate that sleep disturbance is not only associated with experimental measures of EF, performed in an unnatural setting, but that parent reports of executive functioning, which take into account EF in several different naturalistic settings, is also associated with objective measures of sleep disturbance.

These findings somewhat contrast with the results of Study 1, which did not find any associations between actigraphy sleep variables and parent reports of behaviour. However, in line with Study 2, Study 1 also found that increased parental reports of

sleep problems were associated with increased parental reports of behaviour problems, as reported using both the SDQ and the BRIEF.

9.2.3. Study 3: Sleep and Neuropsychological Functioning in Children with Cystic Fibrosis

Study 3 was a replication of Study 2 but used a sample from a population of children deemed to be at risk of sleep disturbance due to underlying respiratory disease. Children with CF were chosen as a suitable population to study because a search of the literature showed very few studies examining sleep in children with CF, and no studies that examined neuropsychological functioning in this group, despite evidence demonstrating poorer sleep efficiency and impaired neurocognition in adult patients with CF (Dancey et al., 2002). The rationale for the study was to enable a further investigation of the model developed by Beebe & Gozal (2002) who propose sleep disturbance and nocturnal hypoxia as two mechanisms that have a detrimental effect on the prefrontal cortex, which then leads to EF deficits. A criticism of the model is that it does not identify the relative importance of the two mechanisms. It was proposed that children with CF could be at risk of nocturnal hypoxia due to night-time symptoms associated with their disease. However, Study 3 did not find significant differences in either the sleep parameters (either actigraphy or oximetry) or neuropsychological functioning of children with CF when compared to the control children reported in Study 3. These results could have been due to the lack of severe respiratory disease in the sample of children with CF, as most children were diagnosed with normal-to-mildly impaired lung function. Furthermore, when children with CF were dichotomised into high and low sleep disturbance groups, neither GEF nor processing speed was significantly better in the low sleep disturbed group.

Of particular interest from Study 3 was the finding that EF was worse in children who were categorised as having either a possible or probable diagnosis of nocturnal hypoxia, irrespective of the level of sleep disturbance. All children with oximetry data (those with and without CF) were divided into two groups – nocturnal hypoxia or no hypoxia. Children in the hypoxia group had significantly lower GEF than children with no hypoxia; being categorised as either high or low sleep disturbance had no effect on the results. These findings are somewhat perplexing as the findings from typically developing children suggest that sleep disturbance, in the absence of hypoxia, is a risk factor for executive dysfunction. In contrast the data from the children with CF suggest

that hypoxia during sleep is main cause of executive dysfunction. One potential explanation for these findings could be that although sleep disturbance contributes to executive dysfunction, when hypoxia is also present the effects of sleep disturbance are no longer relevant for executive dysfunction. Alternatively, it could be that the methodology used to categorise sleep disturbance (i.e. the actigraphy) is not accurately identifying children with and without sleep disturbance.

9.2.4. Study 4: A PSG Study of Children with CF

The final empirical study was aimed at examining in greater detail the night-time respiratory parameters of children with CF using PSG. Originally this study had planned to include a sample of 20 children, but only managed to recruit nine children who underwent one night of full PSG. When compared to published data of healthy children, sleep architecture did not differ in children with CF. No associations could be found between neuropsychological performance and either sleep architecture or respiratory parameters. A major difficulty with the data analyses in Study 4 was the lack of adequate sample size to allow any appropriate comparisons to be made.

9.3. Integration of Key Findings to Previous Literature

9.3.1. Executive Function and Sleep in Healthy, Typically Developing Children

9.3.1.1. Sleep and individual task performance: integration to previous research

Previous studies of sleep and neuropsychological functioning in healthy, typically developing children are limited. Studies have typically only looked at a limited number of cognitive abilities, whereas this thesis attempted to encompass a broad range of abilities deemed executive functions. Study 2 found significant associations between sleep duration and verbal fluency, planning, and working memory. This supports the findings of Randazzo et al. (1998) who demonstrated deficits in verbal creativity and the WCST following sleep restriction in children. However, the study by Randazzo et al. (1998) was experimental manipulation of sleep time conducted in the laboratory, and as such they are able to infer possible a cause and effect mechanism. In contrast, the studies presented in this thesis are correlational, and as such one cannot make conclusions about causality. The results of Study 2 are partially consistent with the findings of Steenari et al. (2003) who found significant associations between working

memory and sleep duration. Steenari et al. (2003) report fairly consistent associations between sleep efficiency and sleep duration with auditory and visual working memory at higher memory load levels. In contrast, this thesis did not find consistent associations between working memory performance and sleep efficiency or sleep duration.

Sadeh, Gruber, and Raviv (2003) also found that attention was better in children who spent longer asleep. This was an experimental manipulation of sleep time, although in contrast to Randazzo et al. (1998), it was not conducted in a controlled environment, however sleep time was measured objectively using actigraphy. Children who extended their sleep time by nearly one hour, performed significantly better on a test of sustained attention, compared their baseline performance. Whereas children who restricted their sleep time by about one hour (and children who had no change in their sleep time) did not improve their performance from baseline to postintervention. However, Sadeh et al. (2003) did not find that performance on the working memory task (digit backward test) was significantly improved from baseline to postintervention in children who extended their sleep time, but they did find that performance on the non-executive task – digits forward – was significantly improved from baseline to postintervention. This is in contrast to the findings of this thesis, which demonstrated an association between increased sleep time and better performance on backward digit recall but not on (forward) simple digit recall. However, this finding was only demonstrated in the typically developing sample in Study 2 and was not reproduced in the CF sample examined in Study 3, possibly as a consequence of the small sample size in Study 3. Furthermore, the studies in this thesis were correlational, and only an experimental design could determine whether increasing sleep time would result in improved neuropsychological performance.

9.3.1.2. Aggregated measures

Performance on many of the individual EF tests was not associated with individual sleep outcome measures. This is not wholly unexpected given that previous studies have not found identical or consistent associations between sleep variables and performance deficits. Randazzo et al. (1998) found deficits in verbal creativity but not memory and learning, Sadeh, Gruver, & Raviv (2003) found deficits in attention but not working memory. From the SDB literature, Lewin & Dahl (2002) did not find an association between SDB and cognition in contrast to both O'Brien et al. (2004) and Blunden et al. (2000). A fundamental distinction between this thesis and previous studies (both the

literature on general sleep disturbance and SDB) was the use of aggregated measures to assess whether the deficits in EF associated with sleep disturbance were general rather than specific. In Studies 2 and 3, this aggregated score (GEF) encompassed performance on tasks purported to measure working memory, sustained attention, verbal fluency, planning, and behavioural inhibition – which represent executive functions proposed by Beebe & Gozal (2002) to be affected by OSA. The novel findings of this thesis were that the aggregate GEF score was much lower in children classified as having high sleep disturbance. This is an important finding as it suggests that sleep disturbance may negatively affect a range of executive functions, and not just one or two specific areas. This is also supported by the data from the children with CF who also had better overall GEF if they were classified as low sleep disturbed. Although the difference was not statistically significant, it was in the expected direction and suggests a substantial effect size of 1.6 *SD*. There were few significant associations when sleep variables and neuropsychological variables were compared; this suggests that in typically developing children, the effect of sleep disturbance on EF may be subtle, so that investigation of any one particular EF may not expose differences between children with and without sleep disturbance. Different measures may also be differentially sensitive to the effects of sleep disturbance. For example, as already noted above, the backward digit recall task used by Sadeh, Gruber, & Raviv (2003) was not sensitive to sleep loss or sleep extension, in contrast to the backward digit recall task used in this thesis.

9.3.1.3. The importance of sleep quantity

Another important finding from Study 2 is the suggestion that sleep *quantity* measures may have greater value as indicators of sleep disturbance than sleep *quality* measures – at least where actigraphy is used to measure sleep. The current literature does not clearly specify or agree which actigraphy values are of most importance when examining sleep disturbance in children and, to the best of my knowledge, no published study has endeavoured to ascertain the relative importance of sleep efficiency and sleep duration on neuropsychological functioning. Some studies have examined sleep minutes and sleep efficiency (Steenari et al., 2003) whereas other studies have only reported sleep efficiency (Amin et al., 2005) or sleep duration (Nixon et al., 2008). The findings in this thesis suggests that when using actigraphic methodology, variables that indicate sleep quantity such as sleep duration and actual sleep minutes, may have greater value as a measure of sleep disturbance compared to sleep efficiency.

9.3.1.4. Sleep and behaviour

In support of the previous literature a consistent finding throughout this thesis has been that parents who rate their children as having sleep problems are more likely to rate their child as having conduct problems and hyperactivity. Furthermore, this thesis adds to the previous literature on healthy, typically developing children, by demonstrating an association between sleep disturbance measured objectively and increased rates of behaviour problems, whereas previous literature has only examined parental reports of sleep problems and behaviour difficulties in typically developing children. Smedje, Broman, & Hetta (2001) found parental reports of emotional symptoms (using the SDQ) were associated with difficulties falling asleep. They also found that conduct problems were higher in children with greater bedtime resistance, and that hyperactivity was associated with more tossing and turning during sleep. In Study 1, conduct problems and hyperactivity were significantly associated with increased parental reports of problems with sleep duration. In Study 2, children who spent longer falling asleep (as measured using actigraphy and parental report) also had increased rates of emotional symptoms and hyperactivity. Higher conduct problems were also reported in children who had increased rates of bedtime resistance (as measured using the CSHQ), and shorter sleep times and lower sleep efficiency as measured using actigraphy. Previous research has also demonstrated an association between SDB and increased rates of hyperactivity (Gottlieb et al., 2003; Chervin et al., 2003) and conduct problems (Chervin et al., 2002; Gottlieb et al., 2004). The present findings have demonstrated these associations in the absence of any known SDB. The similarities in the findings of the SDB and the general sleep disturbance literature suggests there may be parallels in the mechanisms or pathways underlying the association between sleep problems and increased conduct problems.

9.3.1.5. Multi-informant methodology

The studies presented in this thesis also extend the previous literature by incorporating objective and subjective measures of sleep measurement. To the best of my knowledge, previous studies have measured sleep using either parental report or actigraphy/polysomnography, and have not utilised a multi-informant approach. This design enables pervasive aspects of sleep disturbance to be measured through parental report, but also ensures that any factors that may be missed by parents (such as night wakings) are not overlooked.

9.3.1.6. Implications for Beebe & Gozal's model (2002)

Beebe & Gozal (2002) proposed a model to explain the link between OSA and neurocognitive deficits in terms of prefrontal dysfunction. As shown in figure 11, the model indicates two mechanisms during sleep that could be responsible for prefrontal dysfunction- sleep disruption and hypoxia. The model does not specify the relative importance of the two mechanisms and given that previous research suggests that either mechanism in isolation could contribute to prefrontal dysfunction, further clarification of the model is needed. The findings presented in this thesis add further insight into the nature of this relationship as they demonstrate an association between deficits in a range of executive functions and sleep disturbance, in the absence of hypoxia. This finding is of significance to the literature examining SDB and neuropsychological functioning in children because it has typically been assumed that any neuropsychological deficits found in children with SDB can be attributed to the mechanisms of hypoxia. However, as previous literature has shown, and now subsequently supported by the findings of Study 2, neuropsychological deficits can be demonstrated in children with no known hypoxia.

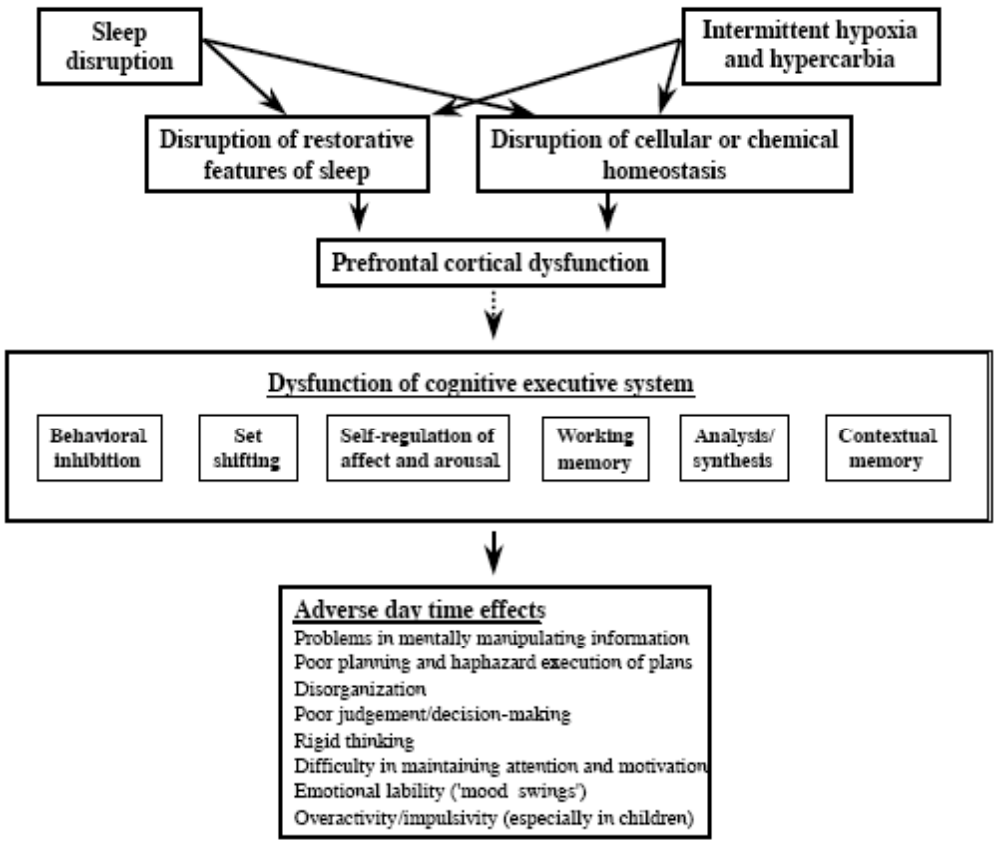

Figure 11 Beebe & Gozal (2002) model of OSA and prefrontal dysfunction

However, there is the possibility that some of the control children in Study 2 had an undiagnosed SDB problem. The use of overnight pulse oximetry in this group was designed to minimize this issue, however, several methodological issues led to only about half of the sample having full oximetry data. Of those children with oximetry data, only two were categorised as having a possible diagnosis of SDB (they had one respiratory parameter outside the recommended normal range), however neither of these children were reported to snore, indicating that the sample was relatively free of any significant SDB or nocturnal hypoxia.

The findings from Study 3, however, indicate that hypoxia has a specific effect on EF, independent of sleep disturbance. In that study children (with and without CF) were divided into a hypoxia and no hypoxia group. Children in the hypoxia group had significantly lower GEF scores compared to children in the no hypoxia group, irrespective of whether they were classified as having high or low sleep disturbance. In contrast, the results for processing speed showed that sleep disturbance, but not hypoxia, had an effect on processing speed. Children in the high sleep disturbance had lower processing speed compared to children in the low sleep disturbance group, irrespective of hypoxia status, although this just failed to reach significance.

9.3.2. Executive Function and Sleep in Children with CF

Studies 3 and 4 have contributed to the existing literature regarding sleep in children with CF. Although the sample sizes in both cases were small and the children were in the lower range of lung disease severity, only a handful of studies have examined sleep in children with CF and none, to the best of my knowledge, have explored neuropsychological nor behavioural functioning in this population. However the results are not wholly consistent with previous findings. Amin et al. (2005) found lower sleep efficiency and more night wakings in children with CF compared to controls. In contrast, this thesis did not find any significant differences in sleep (measured using actigraphy) of children with CF compared to controls. As discussed in Chapter 7, the discrepancies between this study and previous studies could be a consequence of differences in disease severity, age, or data analysis methods. The sample used by Amin et al. (2005) ranged in age from 8 to 18 years, in contrast to this study that used a much smaller range of 6 -12 years. Children with CF did not have greater deficits in GEF or processing speed when compared to the controls, hence the results indicate that

children with CF and normal – moderate lung function may not be at risk of sleep disturbance nor of neuropsychological deficits associated with sleep disturbance.

9.3.2.1. Polysomnography findings

The findings of Study 4 were also partly consistent with the previous literature. Sleep efficiency was not significantly different from the normative data published by Verhulst et al. (2007) or the data on children with CF by Naqvi et al. (2007). However, sleep efficiency in Study 4 was higher than the CF data published by Naqvi et al. (2007) but failed to reach significance; a larger sample may have been able to detect a significant difference. The data presented in Study 4 may have been more similar to the normative sample as the CF children had normal-moderately impaired lung function, whereas in the study by Naqvi et al. (2007) children had moderate-severe lung disease. Sleep latency in the children from Study 4 was significantly different to both the normative data and the CF data. This is most likely a consequence of the different methods used to define sleep-onset. The results of Study 4 also suggest previous findings that children with CF spend a greater percentage of their sleep time in REM sleep (Naqvi et al., 2007), although the reasons for this are unclear.

9.3.3. Sleep and Processing Speed

Although processing speed is not an EF, the decision to include a measure of processing speed in Study 2 was taken on the basis of new findings suggesting that SDB may impact on processing speed performance (Hill et al., 2006). Given that all the tests of EF used in this thesis incorporate a time element, the time taken to execute cognitive processes will invariably have an impact upon performance.

In Study 2, better processing speed was associated with longer sleep duration but this association was not found in the CF children. Furthermore, as already noted above, children with low sleep disturbance had significantly higher processing speed compared to children with high sleep disturbance. In the CF sample, this just failed to reach significance. These novel findings indicate that sleep disturbance has important consequences for processing speed, however the nature of the relationship is unclear. The current literature is focussed on the relationship between sleep and EF, with almost no mention of the effects of sleep on processing speed, particularly in children with no underlying medical condition - Blunden et al. (2000) report processing speed performance for children with SDB. Given that processing speed underlies performance

on many cognitive tasks such as working memory performance (Fry & Hale, 1996), further studies need to examine whether deficits in processing speed underlie the association between sleep and EF, rather than deficits in EF per se.

9.4. Design and Methodology Limitations

9.4.1. Sample Characteristics

A limitation of both studies 1 and 2 concerns the representativeness of the sample to the general population. In both studies, the response rate was typically about 10%. Unfortunately information about non-responders was not available, so it is not possible to ascertain what demographic differences there were between responders and non—responders. Many parents who made initial contact anecdotally reported that their child had sleep difficulties and several children had to be excluded from studies 1 and 2 due to underlying psychopathology, such as ADHD. In contrast, the response rate for the sample of children with CF was much higher. Furthermore, it was noted that several families did not participate because the child was unwell. Consequently, the final sample consisted of a group of children with CF who may not be representative of the population from which they were taken.

9.4.1.1. Sample size limitations

A limitation of all the studies concerns the sample size. Future studies would benefit from larger samples, particularly the sample of children with CF who were recruited from Southampton General Hospital. Originally, Study 3 was to include a second region, which would have increased the number of suitable children with CF, however, issues concerning the R&D process meant that R&D approval took seven months. Constraints around the use of the equipment and the sleep laboratory meant that it was no longer possible to include participants from this second centre.

9.4.2. Measurement Issues

9.4.2.1. Issues in the measurement of sleep

The validity of actigraphy to measure sleep has been subject to debate. Although the methodology is recommended by the American Academy of Sleep Medicine as a useful adjunct in the assessment of sleep disorders, some researchers argue that it is unreliable

as an accurate sleep-wake indicator and it is incorrect to assume that inactivity should be defined as sleep (Pollak et al., 2001). Actigraphy is reliant on this assumption – that inactivity during time in bed represents sleep and therefore activity during time in bed represents wakefulness. Hence, there is the possibility that periods of quiet wakefulness are incorrectly scored as sleep and, vice versa, that movement during sleep may be coded as wake. Individual differences in the amount of movement during sleep are quite feasible; some children may move around a lot during sleep, whereas other children may be less active in their sleep. Some children may be more likely to lie motionless than other children. These factors may result in inaccurate interpretation of actigraphy recordings indicating poor sleep efficiency from waking during the night. Similarly, some children may lie awake and motionless at night, with the actigraph incorrectly reporting sleep times longer than in reality. Another criticism of actigraphy is that it does not give an objective assessment of sleep latency, as this parameter also requires an accurate report from the user regarding the time of going to bed. Hence, although actigraphy is useful for measuring sleep over several nights in the home environment, caution must be used when interpreting certain variables.

9.4.2.2. Issues in the assessment of executive function

As discussed in Chapter 3, the measurement of EF is fraught with methodological issues, particularly in childhood. Any test purporting to measure a 'single' executive function will invariably draw upon other cognitive abilities; hence performance on that task will also reflect other executive and non-executive abilities. As noted above, the speed with which a child processes information will affect performance on cognitive tasks, particularly those that have a time element, which most EF tasks do. This thesis attempts to account for this issue by examining aggregated scores of EF, rather than just examining single executive processes in isolation.

As noted in Chapter 5, the aggregation of EF measures was an attempt to capture the common variance across the EF measures. There was no strong theoretical reason to expect that sleep disturbance would have a greater effect on any particular subsystems of executive function in comparison to others. As noted in the introduction, there is debate concerning whether executive function should be conceptualized as a single process (Baddeley, 1997) or as a collection of processes (Hughes & Graham, 2002). If executive function is a collection of inter-dependent subsystems, one might expect high inter-correlation between the individual subtests. Cronbach's α for the three executive

function tests used in the aggregate in Study 1 is .442, and .589 for Study 2. These values of alpha are not particularly high as values over .7 are usually regarded as satisfactory (Bland & Altman, 1997). However, the value of α will depend on the number of items in the scale - α will increase as the number of items on the scale increases (Cortina, 1993). Furthermore, Cronbach's α is usually calculated when assessing the internal consistency of a large number of items that are attempting to measure the same underlying construct. The aggregation across different executive function tasks was an attempt to capture the common variance in a set of, what were proposed to be, rather different measures of EF. The finding that Cronbach's alpha was not particularly high for these three EF tasks, lends supports to the proposal of Miyake et al (2000) that executive function should be conceptualized as a set of inter-related, but distinct, processes rather than a single process.

Another issue regarding the measurement of EF concerns whether performance on any test of EF is a true reflection of a child's performance in naturalistic situations, such as the classroom. In the classroom, there can be several distractions from other children's behaviour. In contrast, the testing situation is somewhat artificial as it necessitates a quiet, distraction free environment. As such, a child's performance on EF tasks may not accurately reflect how they will function in school.

In Study 1, the CANTAB was used to measure EF, however it was noted that children did not respond well to these tests and often did not fully understand what was required in some tests. However, the CANTAB has been recommended for use in children as young as four, and the reason for this discrepancy is not clear. In the remaining studies, subtests from the TEA-Ch were used, as well as tests from the NEPSY. Both of these tests were originally developed for use with children and virtually all children enjoyed taking part in these tests.

Another limitation of this thesis is that EF was measured in the home environment. It would have been preferable to conduct the cognitive testing in a laboratory setting so that all participants were tested in a consistent environment where distractions were minimised. However, it was considered that families may have been discouraged if they had to travel to take part – some participants were recruited from as far as 40 miles away, particularly Study 3 that recruited children with cystic fibrosis.

9.4.3. Implications for Clinical Practice

The finding that healthy, typically developing children with no obvious hypoxia can have EF deficits that are associated with increased sleep disturbance highlights a need to improve children's sleep hygiene in the general population. Although most parents are probably aware that sleep is important to the well-being and daytime functioning of their child, parents may not be aware of the neuropsychological consequences of sleep disturbance. Health professionals and schools could be encouraged to stress the importance of good sleep practices in children. Data from an Australian cohort (Dollman, Ridley, Olds, & Lowe, 2007) suggests that over the last twenty years, there has been a significant reduction in the sleep duration of children aged 10-15 years, largely as a consequence of later bed-times.

Of significance to respiratory physicians is the finding that not all children with CF have sleep disturbance. Previous research has indicated that children with CF are at risk of sleep disturbance, however such a risk was not demonstrated in this thesis. As discussed in Chapters 7 & 8, the sample of children with CF had well-controlled illnesses, reducing the possibility that nocturnal symptoms would impede the sleep process. Nonetheless, this information will be of interest to families who may be concerned that sleep or neuropsychological functioning will be affected in children with CF. The results of this thesis could be used to reassure parents of children with CF that they are no more at risk of EF deficits than normally developing healthy children if lung function is not severely affected.

9.4.4. Future Directions

The findings of this thesis require further investigation. Additional home-based studies of actigraphy would benefit from a larger sample of children with CF. Improved procedures to ensure a more extensive use of pulse oximetry in home-based studies is also necessary to have confidence that possible nocturnal hypoxia is eliminated in control children. Actigraphy testing was conducted for about 1 week, and included weekend nights and school holidays for some children. Due to the time constraints of a PhD this was unavoidable. Future research could benefit from ensuring that actigraphy testing is conducted during school weeks only. Weekend nights should be included although it may be valuable to examine differences between week and weekend nights. Testing was conducted in the home, and although steps were taken to ensure that this environment was free from distraction, this was not always feasible (e.g. the ringing of a

telephone or a dog barking). Further studies should conduct EF testing in a laboratory setting. Studies 1-3 would also have benefited from obtaining teacher reports of behaviour problems as both the SDQ and the BRIEF are available in teacher-report form. Studies have shown that teachers and parents often do not agree in their assessment of child behaviour. For instance, studies of children with ADHD often show low agreement between teachers and parents ratings of ADHD symptoms (Wolraich et al., 2004). This may not be due to observer error, but rather a consequence of the fact that child behaviour may vary across contexts. Hence obtaining both teacher and parent reports would have ensured that any identified behaviour difficulties are pervasive and not situational. Schools were not approached to obtain teacher reports as it was very difficult to find schools to agree to distribute information about the studies, and it may have been a further deterrent to assisting with recruitment if they had additional obligations to the study.

Further research is needed to explore the model proposed by Beebe & Gozal (2002) and should utilise stringent techniques to ensure that any healthy control children are properly assessed with overnight PSG to exclude any sleep disorder. Future PSG studies would also benefit from including age and sex matched healthy controls to allow a more appropriate comparison for the children with CF. To consider the relative importance of sleep disturbance and hypoxia proposed in Beebe & Gozal's (2002) model it would be beneficial to compare children who are at risk of sleep disturbance, but who do not have any respiratory related illness, to children who have respiratory related disease. For instance children with eczema are at risk of sleep disturbance from night-time scratching, but should not have any respiratory problems. It could be of interest to compare the neuropsychological functioning of such a population to children with SDB, to ascertain whether any deficits in EF are comparable.

Studies also need to examine different and tighter age ranges. This thesis examined children aged 6 – 12 years, but future studies need to examine the impact of sleep disturbance on EF in younger pre-school children and perhaps more importantly in adolescents. Sleep habits in the teenage years are notoriously disturbed, at a time when adolescents are engaging in invaluable school learning.

Longitudinal studies also need to examine whether the neuropsychological effects of sleep disturbance are permanent, or whether executive functioning is improved if the

sleep process becomes less disturbed. As discussed in the introduction (2.7) the mechanisms by which sleep quality/quantity may affect cognition and behaviour are poorly understood. Beebe & Gozal (2002) suggest that the developing brain may be particularly vulnerable to the effects of sleep disturbance due to immaturity of the prefrontal cortex. Sleep disturbance in the early years may cause permanent injury or insult to the prefrontal cortex, which would imply that any impact on EF would also be permanent. However, many developmental neuropsychologists argue that neural plasticity within the developing brain has a protective effect (Huttenlocher, 2002; Thomas, 2003). Hence, it is possible that any damaging effects of sleep disturbance on children's neuropsychological functioning can be restored. Future research would need to identify whether there is a critical period, after which sleep disturbance in children causes permanent damage to the prefrontal cortex.

Future research also needs to examine what factors contribute to the sleep disturbance that subsequently has a negative impact on executive functioning. As discussed in the introduction, sleep disturbance in children can be caused by a variety of factors. As well as the many sleep disorders that can often be diagnosed and treated (such as OSA treated with adenotonsillectomy) there are numerous social, environmental, and parental factors that may not only be harder to identify but also to rectify.

9.4.5. Concluding Remarks

This thesis examined the association between sleep disturbance and neuropsychological functioning in healthy, typically developing children, and children with cystic fibrosis. The findings suggest that sleep disturbance is associated with a global deficit in executive function, deficits in processing speed, and increased conduct problems. Sleep time, as opposed to sleep efficiency, was a better predictor of executive function performance. These findings have implications for children's development; future research examining the effects of sleep disturbance on executive function should consider whether these effects are irreversible.

Appendix A. Study 1 Additional Information

Appendix A.1. Study 1 Invitation to Participate

Mrs Simone Holley
School of Psychology
University of Southampton
Highfield
Southampton
SO17 1BJ

Tel: 02380 594593 or xxxxxxx
email: slh604@soton.ac.uk

Dear Parent
Research is being conducted at the University of Southampton that examines how children's memory and attention may be affected by the amount and the quality of the child's sleep. This is because previous research suggests that sleep provides important rest for the part of the brain that deals with memory, attention, and other cognitive abilities. Previous research has also suggested that poorer memory performance is related to a lower quality of sleep.

We are looking for children aged between 7 (or who are 6 and will have their 7th birthday by April 2006) and 11 years to participate in this current study (please note that we are not looking for children with any particular sleep pattern or memory ability). For three days (and nights) your child will be asked to wear an actigraph: a small watch-like device that measures body movements. It is worn on the wrist and very little discomfort or interference in daily life would be experienced. The child would also perform a variety of computer-based tasks that would assess his or her memory and attention, this would take approximately 1 hour and would be performed in your home (a home computer would not be required). A parent or main carer would be required to complete three questionnaires that should take no more than around 30 minutes in total: these consist of a questionnaire about the child's sleep habits, a questionnaire about your child's memory and attention in everyday situations, and also a questionnaire about your child's general behaviour.

All information regarding you and your child would be kept in the strictest confidence and any published data would not include your name or other any identifying characteristics. This study has been approved by the Ethics Committee in the School of Psychology, at the University of Southampton, who may be contacted on 02380593995.

If you would like to take part in this study or you would like more information please do not hesitate to contact me on the telephone number or email address above. Any help you are able to give will be much appreciated,

Yours Faithfully

Simone Holley

Appendix A.2. Study 1 Participant Information Sheets

Sleep and Memory in Children

Information sheet for parents

This study is being conducted by Simone Holley, a postgraduate research student at the University of Southampton, who is supervised by Professor Jim Stevenson. The study aims to examine whether there is a relationship between children's sleep and their memory and attention. If you consent for your child to take part, your child will need to wear an actigraph, a small, lightweight, watch-like device that would be worn on the wrist. Simone will come to your house on a date convenient to you, in order to give your child the actigraph, which would then be worn for 72 consecutive hours (it can be taken off to bath/shower). During this time it would be helpful if you could record the time your child went to bed and got up in the morning, as well as record the times when the actigraph was taken off. At the end of this period, Simone would return to for the actigraph, and also to conduct the memory and attention testing. This will involve a portable computer, which will be used to administer approximately 1 hour of memory and attention tasks to your child. Children often find these tests enjoyable but your he or she would be free to take a break at any time, or, if necessary, to complete the tasks on another day. Whilst your child completes the tasks you would be asked to complete three questionnaires: a child's sleep habits questionnaire; a questionnaire about your child's memory and attention; and questionnaire about your child's general behaviour. After this, no further participation would be anticipated.

Your child's participation is voluntary and you may withdraw your child at any time during the study without giving reason.

Personal information will not be released to or viewed by anyone other than researchers involved in this project. Results of this study will not include your or your child's name, or any other identifying characteristics.

This study has been approved by the School of Psychology Ethics Committee at the University of Southampton. If you have any questions about your rights as a participant then you may contact them on 023 8059 3995.

If you have any further questions, or to request a summary of the findings then please do not hesitate to contact me, Simone Holley, at the University of Southampton on 02380594593, or email slh604@soton.ac.uk.

Sleep and Memory in Children

Information sheet for child

I am Simone, a student at the University of Southampton where I study children and psychology (why people behave in different ways). I would like to find out if your sleep affects how well you can remember and pay attention to things during the day.

I will ask you to wear a special watch (called an actigraph) for three days. This will tell me how much you move around when you are sleeping.

After this I will come to your house with a computer and ask you to do some tasks using the computer, you do not need to know how to use a computer to do these tasks. This will take about 1 hour, but you can take breaks if you need to.

You can say at anytime if you want to stop taking part, either when you are wearing the watch or doing the computer tasks. You will not get into trouble if you decide to stop.

Your Mum or Dad must also say that it is OK for you to take part.

You can ask me any questions about this if you want to. I hope you have fun taking part!

Sleep and Memory in Children
Research participation consent form for parent

Name of child: _____

Please circle yes or no as appropriate

1. I confirm that I have read and understood the information sheet for the above study and that I have had the opportunity to ask questions. Yes No

2. I understand that my child's participation is voluntary and that I am free to withdraw my child at any time, without giving reasons. Yes No

3. I agree to allow my child to participate in the above study. Yes No

4. I give consent to release information about my child. Yes No

5. I understand that data collected as part of this research project will be treated confidentially, and that published results of this research project will maintain my child's confidentiality. Yes No

Name of parent _____

Signature of parent _____Date _____

Sleep and Memory in Children
Consent form for child

Name of Researcher: _____

Name of child: _____

I have seen the piece of paper about the sleep study

I understand what it says

I would like to take part in the study

I know that I can stop at any time if I want to

_____ _____

Child's signature Date

Appendix A.4. Study 1 Supplementary Data

Table 36 Kolmogorov-Smirnov test of normality for main DV's

	D	df	*p*
Activity index	.103	44	.200*
Long wake episodes	.070	44	.200*
Sleep efficiency	.064	44	.200*
Wake after sleep onset	.064	44	.200*
Total sleep minutes	.098	44	.200*
Sleep latency	.119	44	.125
Child Sleep Habits Questionnaire total	.175	53	.000
Strengths & Difficulties total score	.167	52	.001
BRIEF total score	.118	52	.070
Aggregate Executive Function Score	.088	41	.200*

* This is a lower bound of the true significance.

Table 37 Means and SD of Actigraphy

	Male (n = 24)		Female (n= 19)		*t* test (*df* = 41)	
	Mean	*SD*	Mean	*SD*	*t* value	*p* value
Activity index	51.77	9.12	46.52	9.20	-1.86	0.070
Long wake episodes	5.43	2.56	5.71	3.04	0.33	0.745
Sleep efficiency	85.18	5.89	84.10	6.89	-0.55	0.584
Wake after sleep onset	85.67	34.42	90.14	39.21	0.40	0.693
Total sleep minutes	494.44	39.02	477.02	65.46	-1.08	0.285
Sleep latency	38.79	23.93	40.27	21.81	0.21	0.836

Table 38 Mann Whitney tests of CSHQ scores by gender

	Female (n = 28)		Male (n = 25)		*U* test	
	Median	*IQR*	Median	*IQR*	*U*	*p**
Bedtime Resistance	7.00	2.00	7.00.	1.00	316.50	.525
Sleep Onset Delay	1.00	2.00	1.00	1.00	315.00	.470
Sleep Duration	3.00	2.00	4.00	2.00	348.50	.977
Sleep Anxiety	4.00	2.00	4.00	2.00	342.50	.884
Night Wakings	3.00	1.00	3.00	1.00	324.00	.579
Parasomnias	9.00	2.00	9.00	2.00	331.00	.729
Sleep-Disordered Breathing	3.00	0.00	3.00	1.00	333.50	.688
Daytime Sleepiness	9.00	5.00	8.50	5.00	323.00	.627
Total CSHQ	37.00	10.00	40.00	6.00	344.00	.914

* Asymptotic significance

Table 39 Mann Whitney tests of CANTAB results by gender

	Female (n = 29)		Male (n = 25)		*U* test	
	Median	*IQR*	Median	*IQR*	*U*	*p**
SWM total errors	45.00	47.00	39.00	24.00	299.50	.670
SWM strategy score	35.00	8.00	36.00	6.00	315.50	.902
IED stage reached	9.00	2.00	9.00	2.00	320.50	.412
IED total errors	47.00	44.00	24.00	35.00	325.00	.515
SOC minimum moves	7.00	3.00	7.00	4.00	328.00	.545
PRM correct	22.00	3.00	22.00	3.00	346.00	.942
SSP span	5.00	1.00	5.00	0.00	300.00	.232
RVP A’	0.95	0.06	0.95	0.07	334.00	.621
RVP B’	0.90	0.19	0.83	0.28	222.00	.015
RVP latency	424.23	142.75	391.45	177.39	338.00	.671

* Asymptotic significance
(SWM = Spatial Working Memory, IED = Intra/Extradimensional shift, SOC = Stockings of Cambridge, PRM = Pattern Recognition Memory, SSP = Spatial Span, RVP = Rapid Visual Processing).

Table 40 Mean SDQ scores by gender

	Female (n = 28)		Male (n=24)		*U* test*	
	Median	*IQR*	Median	*IQR*	*U*	*p*
Emotional Symptoms	2.50	4.00	1.00	3.00	277.50	.272
Conduct Problems	1.00	2.00	1.50	3.00	308.50	.603
Hyperactivity	2.00	4.00	4.50	5.00	236.50	.066
Peer Problems	1.00	3.00	1.00	2.00	330.50	.917
Pro-social scale	9.00	2.00	8.00	3.00	222.00	.033
Total SDQ	6.50	8.00	8.50	10.00	285.00	.348

* Asymptotic significance

Table 41 Mann-Whitney tests of SDQ symptoms of children with high & low sleep disturbance

	High sleep disturbance (n=20)	Low sleep disturbance (n=20)	*U* test	
	Mean (*IQR*)	Mean (*IQR*)	*U*	*p**
Emotional Symptoms	3.00 (4.00)	1.00 (3.00)	156.00	.242
Conduct Problems	1.50 (2.00)	1.00 (2.00)	174.00	.495
Hyperactivity	3.50 (6.00)	3.50 (6.00)	189.50	.779
Peer Problems	0.50 (2.00)	1.00 (2.00)	195.00	.904
Pro-social scale	8.50 (4.00)	8.00 (2.00)	186.50	.718
Total SDQ	8.00 (7.00)	6.50 (13.00)	185.00	.698

*Exact significance

Table 42 Correlations between age, actigraphy, and CANTAB scores (n=40)

	1	2	3	4	5	6	7	8	9	10	11	14	15	16	17	18	19
SWM total errs	1.00																
SWM strategy	**.67**	1.00															
IED stage	-.10	-.17	1.00														
IED total errors	.15	.26	**-.87**	1.00													
SOC min moves	**-.47**	**-.31**	-.03	-.20	1.00												
PRM correct	**-.36**	**-.26**	.04	-.20	.16	1.00											
SSP span	**-.59**	**-.57**	.06	-.17	**.42**	.14	1.00										
RVP A	**-.32**	-.24	.16	-.17	**.33**	.16	**.32**	1.00									
RVP B	-.17	-.20	-.28	.19	**.40**	-.03	.24	-.07	1.00								
RVP latency	**.40**	.26	.12	-.19	-.13	.09	-.25	**-.27**	**-.33**	1.00							
Activity index	-.05	.00	.25	-.06	-.23	.07	-.21	-.13	-.15	.14	1.00						
LWE	.06	.10	.11	-.03	-.29	.08	-.19	-.08	-.20	.22	**.48**	1.00					
Sleep efficiency	-.03	-.01	-.06	.02	.31	-.06	.17	-.11	.22	-.14	**-.50**	**-.21**	1.00				
WASO	.02	.00	.02	.06	**-.31**	.10	-.19	-.11	-.23	.18	**.51**	**.91**	**-.91**	1.00			
Total sleep mins	.09	.18	-.18	.11	.24	-.05	.04	.06	.12	.10	**-.48**	**-.64**	**.81**	**-.76**	1.00		
Sleep latency	.14	.07	.05	-.01	-.25	-.25	-.18	-.22	.00	.13	.27	**.43**	**-.51**	**.46**	**-.42**	1.00	
Age	**-.43**	**-.37**	.29	**-.34**	**.36**	-.16	**.46**	**.42**	.11	**-.54**	-.26	-.24	.17	-.24	.09	.03	1.00

Significant correlations, $p < .05$, shown in bold script

(SWM= Spatial Working Memory; IED = Intra/Extra Dimensional Set Shift; SOC = Stockings of Cambridge; PRM = Pattern Recognition Memory; SSP = spatial span; RVP = Rapid Visual Processing; LWE = Long Wake Episodes; WASO = wake after sleep onset)

Table 43 Means and *SD* of BRIEF scores by sleep disturbance

	Low sleep disturbance (n=20)		High sleep disturbance (n=20)		*t* test	
	Mean	*SD*	Mean	*SD*	*t*	*p*
Inhibit	52.15	8.81	54.30	8.67	-.778	.441
Shift	51.40	11.62	51.10	7.36	.098	.923
Emotional Control	51.05	10.06	52.35	9.28	-.425	.673
Behavioural Regulation Index	52.15	10.02	53.20	8.87	-.351	.728
Initiate	49.75	7.96	51.80	10.28	-.795	.485
Working Memory	54.05	11.56	55.60	13.36	-.392	.697
Plan/Organize	54.90	9.82	54.25	11.90	.188	.852
Org. Materials	58.20	8.74	57.50	6.45	.288	.775
Monitor	54.30	11.76	53.15	11.85	.308	.760
Metacognition index	55.10	9.40	54.35	9.81	.247	.806
Global Executive Control	54.10	9.65	55.00	9.78	-.293	.771

Table 44 *F* ratios and effect sizes for univariate main effects of sleep disturbance on BRIEF subscales

Source		Mean Square	df	*F*	*p*
Multivariate	Sleep disturbance $\lambda = .805$		11	0.76	ns
Univariate					
Sleep quality	Inhibit	48.57	1	0.62	ns
	Shift	0.42	1	0.00	ns
	Emotional Control	34.97	1	0.38	ns
	Initiate	36.30	1	0.43	ns
	Working Memory	12.67	1	0.08	ns
	Plan/Organize	5.83	1	0.05	ns
	Org. Materials	4.31	1	0.07	ns
	Monitor	18.61	1	0.13	ns
	Metacognition	9.74	1	0.10	ns
Error	Inhibit	78.20	36		
	Shift	94.32	36		
	Emotional Control	92.66	36		
	Initiate	85.44	36		
	Working Memory	156.25	36		
	Plan/Organize	124.99	36		
	Org. Materials	61.67	36		
	Monitor	126.09	36		
	Metacognition	93.60	36		

Table 45 Correlations between actigraphy and BRIEF

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Total sleep minutes	1.00																
Sleep efficiency	**.77**	1.00															
LWE	**-.62**	**-.91**	1.00														
WASO	**-.72**	**-.99**	**.91**	1.00													
Sleep latency	**-.41**	**-.50**	**.45**	**.46**	1.00												
Activity index	**-.46**	**-.52**	**.51**	**.52**	**.30**	1.00											
Inhibition	-.06	-.01	.06	.00	-.17	-.19	1.00										
Shift	-.22	-.03	.03	.02	.10	.20	**.52**	1.00									
Emotional Control	-.23	-.02	-.04	.02	-.08	.01	**.64**	**.68**	1.00								
BRI	-.22	-.05	.04	.03	-.04	.08	**.83**	**.82**	**.88**	1.00							
Initiate	.08	.14	-.15	-.12	-.03	.00	**.58**	**.45**	**.49**	**.56**	1.00						
Working Memory	-.03	.00	.08	.01	.02	.19	**.60**	**.53**	**.44**	**.60**	**.76**	1.00					
Plan/Organize	-.17	.01	-.03	-.03	-.05	.02	**.73**	**.61**	**.66**	**.76**	**.76**	**.80**	1.00				
OM	-.11	-.01	.10	-.06	.01	.03	**.34**	**.36**	.22	**.35**	**.47**	**.52**	**.53**	1.00			
Monitor	-.23	-.15	.13	.12	.06	.04	**.74**	**.57**	**.64**	**.76**	**.58**	**.70**	**.83**	**.48**	1.00		
MI	-.19	-.08	.10	.06	.05	.13	**.73**	**.63**	**.61**	**.75**	**.78**	**.82**	**.91**	**.63**	**.83**	1.00	
GEC	-.15	-.01	.02	-.01	-.03	.05	**.81**	**.72**	**.75**	**.87**	**.79**	**.86**	**.94**	**.58**	**.88**	**.94**	1.00

Significant correlations shown in bold ($p < .05$)

(LWE = long wake episodes; WASO = wake after sleep onset; BRI = Behavioral Regulation Index; OM = Organization of Materials; MI = Metacognition Index; GEC = Global Executive Control)

Table 46 Correlations between CSHQ and BRIEF

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
BR	1.00																			
SOD	**.49**	1.00																		
SD	**.50**	**.48**	1.00																	
SA	**.60**	**.46**	**.43**	1.00																
NW	**.42**	**.50**	**.33**	**.57**	1.00															
Para	**.33**	.16	**.33**	**.30**	**.42**	1.00														
SDB	.10	.16	.25	.04	.00	.04	1.00													
DS	**.33**	**.37**	**.32**	**.34**	.14	.17	-.02	1.00												
CSHQ	**.74**	**.64**	**.73**	**.70**	**.57**	**.59**	.21	**.68**	1.00											
Inhib	.20	.17	**.36**	**.29**	.07	**.35**	.08	**.36**	**.43**	1.00										
Shift	.08	.14	.09	.26	**.30**	**.30**	-.13	.20	.26	**.52**	1.00									
EC	.05	.13	.20	.10	.22	**.28**	-.15	**.35**	**.30**	**.64**	**.68**	1.00								
BRI	.13	.17	.26	.25	.27	**.34**	-.04	**.32**	**.38**	**.83**	**.82**	**.88**	1.00							
Initiate	.10	.13	.15	**.34**	.02	.17	-.10	**.46**	**.33**	**.58**	**.45**	**.49**	**.56**	1.00						
WM	.00	.05	.19	.19	.03	.27	-.04	**.31**	.26	**.60**	**.53**	**.44**	**.60**	**.76**	1.00					
Plan	.14	.18	**.28**	**.32**	.16	**.39**	-.07	**.35**	**.40**	**.73**	**.61**	**.66**	**.76**	**.76**	**.80**	1.00				
Org	**.30**	.16	.23	.22	.03	.19	.14	.20	**.31**	**.34**	**.36**	.22	**.35**	**.47**	**.52**	**.53**	1.00			
Mon	.16	.02	**.32**	.19	.12	**.36**	-.07	.27	**.34**	**.74**	**.57**	**.64**	**.76**	**.58**	**.70**	**.83**	**.48**	1.00		
Meta	.17	.17	.27	**.34**	.13	**.34**	-.02	**.38**	**.41**	**.73**	**.63**	**.61**	**.75**	**.78**	**.82**	**.91**	**.63**	**.83**	1.00	
GEC	.14	.14	.27	**.29**	.14	**.37**	-.04	**.39**	**.40**	**.81**	**.72**	**.75**	**.87**	**.79**	**.86**	**.94**	**.58**	**.88**	**.94**	1.00

Significant correlations ($p < .05$) shown in bold script

(BR = bedtime resistance; SOD = sleep onset delay; SD = sleep duration; SA = sleep anxiety; NW = night wakings; Para = parasomnias; SDB = sleep disordered breathing; DS = daytime sleepiness; Inhib = Inhibit; EC = Emotional Control; WM = Working Memory; PO = Plan/Organize; OM = Organization of Materials; Mon = Monitor; MI = Metacognition Index; GEC = Global Executive Control)

Table 47 Associations between CANTAB and BRIEF (n = 49)

	1	2	3	4	5	6	7	9	8	10	11	12	13	14	15	16	17	18	19	20	21
SWM1	1.00																				
SWM2	**.71**	1.00																			
IED1	-.24	**-.28**	1.00																		
IED2	.28	**.37**	**-.89**	1.00																	
SOC	**-.49**	**-.34**	.05	-.19	1.00																
PRM	**-.40**	**-.32**	.16	-.28	.20	1.00															
SSP	**-.57**	**-.48**	.09	-.17	**.49**	.21	1.00														
RVP A	**-.38**	-.30	.28	-.26	**.35**	.19	**.25**	1.00													
RVP B	-.19	.17	-.20	.13	.27	.07	.27	.03	1.00												
RVP L	**-.47**	**.35**	-.14	.07	-.26	-.07	-.27	**-.57**	**-.36**	1.00											
Inhibit	.13	.11	-.01	.01	-.27	-.13	-.28	-.24	-.08	.17	1.00										
Shift	.17	.18	.01	.05	-.24	-.21	**-.30**	**-.32**	-.13	.28	**.52**	1.00									
EC	.17	.12	-.15	.24	-.27	-.16	-.19	**-.30**	-.07	.18	**.67**	**.68**	1.00								
BRI	.15	.15	-.08	.17	-.27	-.26	-.26	**-.30**	-.08	.20	**.83**	**.82**	**.88**	1.00							
Initiate	.23	.19	-.09	.18	**-.32**	-.21	**-.36**	-.21	-.15	.10	**.54**	**.47**	**.49**	**.54**	1.00						
WM	**.35**	**.33**	.05	.04	-.27	-.23	**-.43**	-.25	-.20	.23	**.59**	**.56**	**.44**	**.60**	**.75**	1.00					
P/O	**.35**	.18	-.04	.13	**-.36**	**-.38**	**-.37**	**-.32**	-.21	.19	**.72**	**.65**	**.68**	**.77**	**.74**	**.82**	1.00				
OM	.19	.20	.14	-.07	-.25	-.19	**-.29**	-.07	-.18	.03	**.29**	**.35**	.20	**.31**	**.44**	**.50**	**.51**	1.00			
Monitor	.28	.14	-.04	.09	-.27	**-.35**	**-.36**	**-.40**	-.12	.16	**.73**	**.59**	**.65**	**.76**	**.55**	**.68**	**.84**	**.45**	1.00		
Meta	**.31**	.22	-.02	.07	**-.39**	-.24	**-.41**	**-.33**	-.07	.20	**.72**	**.67**	**.62**	**.75**	**.76**	**.81**	**.90**	**.61**	**.82**	1.00	
GEC	**.31**	.23	-.04	.12	**-.35**	**-.31**	**-.40**	**-.34**	-.17	.22	**.80**	**.75**	**.76**	**.87**	**.77**	**.86**	**.94**	**.55**	**.88**	**.93**	1.00

Significant correlations, $p < .05$, shown in bold script

(SWM = spatial working memory; IED = Intra/Extra Dimensional Set Shift; SOC = Stockings of Cambridge; PRM = Pattern Recognition Memory; SSP = spatial span; RVP = Rapid Visual Processing EC = Emotional Control; WM = Working Memory; PO = Plan/Organize; OM = Organization of Materials; Mon = Monitor; MI = Metacognition Index; GEC = Global Executive Control)

Appendix B. Study 2 Additional Information

University of Southampton

Sleep, Learning, & Behaviour in Children with Asthma and Eczema

Dear Parent / Guardian

You and your child are being invited to take part in a research study that is being conducted at the University of Southampton to investigate the sleep patterns of children who have asthma and/or eczema. It is possible that such children will be more likely to experience sleep disturbance due to night-time symptoms. The study also aims to investigate whether children with sleep disturbance experience difficulties with behaviour and/or learning during the daytime. Previous research has shown that *some* children who experience greater sleep disruption have difficulties with memory and attention.

If you and your child decide to take part, the study would involve your child wearing an actigraph for a week. An actigraph is a small, watch-like device worn on the wrist that measures movement and records activity during sleep, very rarely do children report any discomfort in wearing the watch. A researcher would also undertake a neuropsychological assessment of your child and you would need to complete some questionnaires about your child's behaviour and sleeping patterns. We would also ask your child to keep a record of their daily symptoms. We also need to find children who do not have asthma or eczema to take part in the study, we would therefore ask if your child has a friend of similar age, who does not have any allergic disease, and who would be interested in taking part.

All information regarding you and your child would be kept in the strictest confidence and any published data would not include your name or other any identifying characteristics.

If you would like to take part in this study or you would like more information please do not hesitate to contact me on the telephone number or email address below. Any help you are able to give will be much appreciated,

Yours Sincerely

Simone Holley

Postgraduate Research Student

Tel: 02380 594593
Mob: xxxxxxxxxxxxx
email: Slh604@soton.ac.uk

Appendix B.2. NHS Ethics Approval

Salisbury and South Wiltshire Research Ethics Committee
Room 11
John Apley Building
Royal United Hospital
Combe Park
Bath
BA1 3NG

Telephone: 01225 821031
Facsimile: 01225 825725

21 December 2006

Mrs Simone Holley
Postgraduate Research Student
University of Southampton
School of Psychology
Highfield
Southampton
SO17 1BJ

Dear Mrs Holley

Full title of study: **The relationship between sleep quality, cognition, and behaviour in children who have comorbid asthma and atopic dermatitis**
REC reference number: **06/Q2008/51**

The Research Ethics Committee reviewed the above application at the meeting held on 20 December 2006. The Committee would like to thank you for attending the meeting.

Documents reviewed

The documents reviewed at the meeting were:

Document	*Version*	*Date*
Application	5.2	27 November 2006
Investigator CV	1	31 December 2005
Protocol	1	
Letter from Sponsor		21 November 2006
Compensation Arrangements	Memo	21 November 2006
Questionnaire: Child's sleep habits		
Questionnaire: Allergy Questionnaire		
Questionnaire: Strengths and Difficulties		
Letter of invitation to participant	1	01 November 2006
Participant Information Sheet	1	01 November 2006
Participant Information Sheet: information sheet for child without asthma/eczema	1	01 November 2006
Participant Information Sheet: Information sheet for child with asthma/eczema	1	01 November 2006
Participant Consent Form: Consent form for parent	1	01 November 2006
Participant Consent Form: Child consent form	1	01 November 2006
Sleep Self Report	Child's form	
Additional Information	1	01 November 2006
CV	Jim Stevenson	31 December 2005
BRIEF	Parent Form	

Provisional opinion

The Committee would be content to give a favourable ethical opinion of the research, subject to receiving a complete response to the request for further information set out below.

Authority to consider your response and to confirm the Committee's final opinion has been delegated to The Chair.

Further information or clarification required

(a) The Committee felt that the Patient Information Sheet should contain more detail regarding the time taken to complete the questionnaire and it should also be explained that there are some personal questions.

(b) The Committee felt that the question relating to pets should ask more specifically whether it is cats, dogs, etc.

(c) Can you please provide evidence that the Consultants are happy to support this study.

(d) The committee feel that at question A22 on the application form the bracketed phrase '(3 or more times a week)' should be removed.

(e) On the Patient Information Sheet the Committee feel that reference should be made to 'You and your child have been' and not just 'You have been chosen'.

(f) The response to A57 on the application form should state for example 'University of Southampton standard procedures for sponsors will be followed'.

(g) All reference to Salisbury and South Wiltshire Research Ethics Committee having 'approved' the study must be removed.

(h) At question A56 on the application form it should be stated that you will be using Acute Trusts.

When submitting your response to the Committee, please send revised documentation where appropriate underlining or otherwise highlighting the changes you have made and giving revised version numbers and dates.

The Committee will confirm the final ethical opinion within a maximum of 60 days from the date of initial receipt of the application, excluding the time taken by you to respond fully to the above points. A response should be submitted by no later than 20 April 2007.

Ethical review of research sites

The Committee agreed that all sites in this study should be exempt from site-specific assessment (SSA). There is no need to complete Part C of the application form or to inform Local Research Ethics Committees (LRECs) about the research. However, all researchers and local research collaborators who intend to participate in this study at NHS sites should notify the R&D Department for the relevant care organisation and seek research governance approval.

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

REC reference number 06/Q2008/51 Please quote this number on all correspondence

Yours sincerely

Kirsten Peck

pp **Mrs Katrina Brockbank**
Chair
Salisbury and South Wiltshire Research Ethics Committee

Email: kirsten.peck@ruh-bath.swest.nhs.uk

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments.

Copy to: Dr Martina Dorward Research Governance Office University of Southampton Highfield Southampton SO17 1BJ

Wiltshire Research Ethics Committee
Room 11
John Apley Building
Royal United Hospital
Combe Park
Bath
BA1 3NG

Tel: 01225 821031
Fax: 01225 825725

13 March 2007

Mrs Simone Holley
Postgraduate Research Student
School of Psychology
Highfield
Southampton
SO17 1BJ

Dear Mrs Holley

Study title:	**The relationship between sleep quality, cognition, and behaviour in children who have comorbid asthma and atopic dermatitis**
REC reference:	**06/Q2008/51**
Amendment number:	**3.1**
Amendment date:	**09 February 2007**

The above amendment was reviewed at the meeting of the Committee held on 01 March 2007.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Protocol	1	08 February 2007
Participant Information Sheet: For child with asthma/eczema	2	
Participant Information Sheet	3	08 February 2007
Notice of Substantial Amendment (non-CTIMPs)	3.1	09 February 2007

Questionnaire: Allergy Questionnaire		
Questionnaire: Strengths and Difficulties		
Participant Information Sheet	2	09 January 2007
Participant Information Sheet: information sheet for child without asthma/eczema	1	01 November 2006
Participant Information Sheet: Information sheet for child with asthma/eczema	1	01 November 2006
Participant Consent Form: Consent form for parent	1	01 November 2006
Participant Consent Form: Child consent form	1	01 November 2006
Sleep Self Report	Child's form	
CV	Jim Stevenson	31 December 2005
BRIEF	Parent Form	
e-mail	Robert Scott-Jupp	10 September 2006
e-mail	Deborah Mitchell	10 October 2006
Appendix A	2	09 January 2007
Additional Information	2	09 January 2007

Research governance approval

You should arrange for the R&D department at all relevant NHS care organisations to be notified that the research will be taking place, and provide a copy of the REC application, the protocol and this letter.

All researchers and research collaborators who will be participating in the research must obtain final research governance approval before commencing any research procedures. Where a substantive contract is not held with the care organisation, it may be necessary for an honorary contract to be issued before approval for the research can be given.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

REC reference 06/Q2008/51	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely

Kirsten Peck

pp **Mrs Katrina Brockbank**
Dr Elizabeth Price
Co Chair

Email: kirsten.peck@ruh-bath.swest.nhs.uk

Enclosures: Standard approval conditions

Copy to: Dr Martina Dorward Research Governance Office University of Southampton Highfield Southampton SO17 1BJ

Membership of the Committee

The members of the Committee who were present at the meeting are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

REC reference 06/Q2008/51: Please quote this number on all correspondence

Yours sincerely

Kirsten Peck.

Mrs Kirsten Peck
Co-ordinator
Wiltshire Research Ethics Committee

Enclosures List of names and professions of members who were present at the meeting and those who submitted written comments

Copy to: Dr Martina Dorward, University of Southampto

NHS

National Research Ethics Service

Wiltshire Research Ethics Committee
Room 11
John Apley Building
Royal United Hospital
Combe Park
Bath
BA1 3NG

Tel: 01225 824255
Fax: 01225 825725

11 June 2007

Mrs Simone Holley
Postgraduate Research Student
School of Psychology
Highfield
Southampton
SO17 1BJ

Dear Mrs Holley

Study title:	**The relationship between sleep quality, cognition, and behaviour in children who have comorbid asthma and atopic dermatitis**
REC reference:	**06/Q2008/51**
Amendment number:	**3**
Amendment date:	**01 May 2007**

The above amendment was reviewed at the meeting of the Committee held on 07 June 2007.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation. However on the poster reference to Wiltshire Research Ethics Committee having 'approved' the study must be changed to Wiltshire Research Ethics Coimmittee having 'reviewed' the study.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Protocol	3	01 May 2007
Participant Information Sheet	3 - For child with asthma	01 May 2007
Participant Information Sheet	4 - For Parents	01 May 2007

Reminder postal invitation to participate	1	10 May 2007
Postal invitation to participate	1	10 May 2007
Notice of Substantial Amendment (non-CTIMPs)	3	01 May 2007
Letter of invitation to participant	3	01 May 2007
Advertisement	1	01 May 2007

Membership of the Committee

The members of the Committee who were present at the meeting are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

REC referenc enumber 06/Q2008/51: Please quote this number on all correspondence

Yours sincerely

Kirsten Peck.

Mrs Kirsten Peck
Co-ordinator
Wiltshire Research Ethics Committee

Enclosures List of names and professions of members who were present at the meeting and those who submitted written comments

University of Southampton

School of Psychology

Sleep, Learning, & Behaviour in Children

Information sheet for parents

You and your child have been invited to take part in a research study being conducted by Simone Holley, a postgraduate research student at the University of Southampton, who is supervised by Professor Jim Stevenson, School of Psychology. Before you decide to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Please ask if anything is not clear or you would like more information.

What is the purpose of the study?
The study aims to examine whether attention, memory, and behaviour are affected by sleep disturbance in normally developing healthy children.

Why has my child been chosen?
We are looking for children aged between 6 and 12 years of age.

- History of head injury
- Diagnosis or treatment for ADHD (attention-deficit hyperactivity disorder)
- Other serious medical conditions or disabilities
- Any history of learning difficulties such as dyslexia
- Any history of psychological problems

Do we have to take part?
You and your child's participation is voluntary, it is up to you to decide whether or not you wish to take part, but we would ask that you ensure your child understands what is involved and is willing to take part. If you agree to take part, you will be asked to sign a consent form but you should be aware that even though you sign the consent form, you are still free to withdraw your child from the study at any time without giving reason.

What will happen to my child if they take part?
The study involves your child wearing an actigraph, a small, lightweight, watch-like device that will need to be worn on the wrist for 7 consecutive days and nights. This device measures movement and enables us to examine the amount of disruption to your child's sleep. It can be taken off to bath/shower and for any other activities where necessary. For at least one night of the actigraphy recording, your child would also need to wear a pulse oximeter. This device measures the amount of oxygen in the blood and involves wearing a
sensor on the fingertip throughout the night. If your child does not find the oximeter troublesome after the first night, we would ask that the oximeter is worn for a further two or three nights. At some point during the study, Simone will conduct some

psychological tests with your child that test attention, memory, and learning. Some of these will be paper and pencil tests, and some will be computer based.

What do I have to do?
During the study, you would need to record the time your child went to bed and got up in the morning. There are also some questionnaires for you to complete about your child's sleep, behaviour, and allergy symptoms. In addition, there is also a questionnaire that includes personal questions about you and your partner's employment and educational background. Please note that you are under no obligation to provide answers to any questions. In total, the questionnaires would take 20 minutes to complete. When the neuropsychological tests are carries out you will need to provide a quiet room with a table and chair. It is very important that the tests are conducted with no distractions.

What are the possible benefits of taking part?
At the end of the study, you will be given a summary sheet of what the actigraph records about your child's sleep, and information from the psychological tests. Many children often find wearing the actigraph fun and the psychological tests enjoyable.

Are there any disadvantages of taking part?
The actiwatch has been successfully used in previous studies with children. Very occasionally, a child may be resistant to wearing the watch and find it uncomfortable. Similarly, some children may find the pulse oximeter uncomfortable. In these instances, you can withdraw your child from the study.

Will our personal information be protected?
Personal information will not be released to or viewed by anyone other than researchers involved in this project. Results of this study will not include your or your child's name, or any other identifying characteristics. Procedures for handling, processing, storage and destruction of data is compliant with the Data Protection Act 1998. Data will be stored anonymously and securely on disc for up to 10 years. Only authorized persons will have access to the data.

Contact for further information
If you have further questions contact Simone Holley, at the University of Southampton on 02380594593, email slh604@soton.ac.uk or home xxxxxxxxxx

Thank you for taking the time to read this sheet.

Sleep, Learning, & Behaviour in Children with Asthma and Eczema
Information sheet for child

My name is Simone, I am student at the University of Southampton. I am asking if you would like to take part in my project. I am trying to find out if children who have asthma and eczema do not sleep very well. I would also like to know if children are better at learning when they sleep well. Before you decide to take part, it is important that you understand why the research is being done and what will happen to you. Please read this leaflet carefully and ask your mum or dad anything you do not understand.

Why are we doing this research?
We want to find out if children with asthma and/or eczema have trouble sleeping because of their illness. We also want to know if sleeping badly affects how well children can learn, pay attention, and remember things.

Why have I been asked to take part?
We need to find about 50 children who have asthma and eczema. We also need about 50 children who do not have asthma and eczema to take part.

Do I have to take part?
No! It is up to YOU. You must only take part if you want to, and if your parents are happy for you to take part.

What will happen to me if I take part?
I will ask you to wear a special watch (called an actigraph) for five days. This will tell me how much you move around when you are sleeping. I will also ask you to wear something on your fingertip for one night (or two or three nights if it does not bother you. This tells me how much oxygen is in your blood. I will also come to your house to do some special tasks with you and ask you to fill in a questionnaire about your sleep. This will take about 1 hour and 30 minutes. I will also ask your parents about your sleep and behaviour.

Is there anything for me to be worried about?
A few children sometimes find the watch a little uncomfortable especially if you are not used to wearing a watch. Also, you may find the finger sensor uncomfortable but it will not hurt. Remember, you can say at anytime if you want to stop taking part, either when you are wearing the watch or doing the tasks. You will not get into trouble if you decide to stop.

Will I have fun?
Some children enjoy wearing the special watch and doing the tasks. I hope you will have fun taking part!
If you have any questions or there is anything you don't understand you can ask me or your parents.

University of Southampton

School of Psychology

Sleep , Learning, & Behaviour in Children
Consent form for parent

Name of child: _____

Please initial boxes

1. I confirm that I have read and understood the information sheet for the above study and that I have had the opportunity to consider the information and ask questions. ☐

2. I understand that my child's participation is voluntary and that I am free to withdraw my child at any time, without giving any reasons, and without my child's medical care or legal rights being affected. ☐

3. I agree to allow my child to participate in the above study. ☐

4. I give consent to release information about my child. ☐

5. I understand that data collected as part of this research project will be treated confidentially, and that published results of this research project will maintain my child's confidentiality. ☐

…….	…….	…….
Name of parent/guardian	Date	Parents signature
……. …….	…….	…….
Researcher	Date	Researcher's signature

Sleep, Learning, & Behaviour in Children
Consent form for child

Have you read (or had read to you) about this project?	Yes/No
Has somebody else explained this project to you?	Yes/No
Do you understand what this project is about?	Yes/No
Have you asked all the questions you want?	Yes/No
Have you had your questions answered in a way you understand?	Yes/No
Do you understand it's OK to stop taking part at any time?	Yes/No
Are you happy to take part?	Yes/No

If any answers are 'no' or you **don't** want to take part, **don't** sign your name!

If you do want to take part, please write your name and today's date

Your name _____

Date _____

Name of Researcher: _____

Appendix B.5. SES Questionnaire

Impact of Sleep Quality on Daytime Functioning in Children with Epilepsy
Additional Information

Child's name: .....

Your name: .....

Your relationship to child: .....

1. Which of the following best describes your current marital status?

Married/living with partner ☐ Single ☐ Separated/divorced ☐ Widowed ☐

3. ***What is the highest grade of school you have completed?***

	You	Partner
School to 16, no qualifications	☐	☐
School to 16, GCSE's/O' levels	☐	☐
Sixth form school or college, A' levels	☐	☐
Highers, Scotvec, or NVQ's	☐	☐
University degree	☐	☐
Professional or postgraduate degree	☐	☐

4. Do you have any of the following professional qualifications?
(Tick all the boxes that apply)

☐ Professional Qualifications Qualified Dentist ☐

☐ Qualified Teacher Status (for schools) ☐ Qualified Nurse, Midwife, Health Visitor

☐ Qualified Medical Doctor ☐ Other Professional Qualifications

5. If employed inside or outside the home, what is your job title?

.....

Please describe briefly your main job activities

.....

What is your partner's job title?

.....

Table 48 Study 2 Kolmogorov-Smirnov data

	D	df	*p*
Sleep duration	.046	56	.200*
Total sleep minutes	.092	56	.200*
Sleep efficiency	.106	56	.182
Sleep latency	.099	56	.200*
Long wake episodes	.085	56	.200*
Activity index	.072	56	.200*
Wake after sleep onset	.135	56	.049
Child Sleep Habits Questionnaire total	.094	55	.012
Strengths & Difficulties total score	.096	57	.200*
BRIEF total score	.098	59	.200*
Processing Speed	.046	56	.200*
Global Executive Function Score	.082	52	.200*

* This is a lower bound of the true significance.

Table 49 Actigraphy sleep variables means and *SD* by gender

	Males (n=26)		Females (n=30)		t test (df=54)	
	Mean	*SD*	Mean	*SD*	*t*	*p*
Sleep duration	552.96	36.88	575.25	36.76	2.26	.028
Total sleep minutes	453.78	55.99	495.07	55.73	2.76	.008
Sleep efficiency	82.65	9.07	86.67	6.47	1.93	.059
Sleep latency	54.77	32.61	44.07	29.63	-1.29	.204
Long wake episodes	5.66	3.02	4.57	2.35	-1.52	.134
Activity index	49.89	12.44	44.86	12.60	-1.50	.140
Wake after sleep onset	95.93	50.15	76.43	35.10	-1.70	.094

Table 50 Mann Whitney U tests of CSHQ by gender

	Females (n=32)		Males (n=24)		*U* test	
	Median	*IQR*	Median	*IQR*	*U*	*p**
Bedtime Resistance	7.00	2.00	6.00	1.00	336.00	.393
Sleep Onset Delay	2.00	1.00	1.00	1.00	309.50	.184
Sleep Duration	4.50	4.00	3.50	2.00	310.50	.203
Sleep Anxiety	4.00	2.00	4.00	0.00	316.00	.171
Night Wakings	3.00	1.00	3.00	1.00	358.00	.618
Parasomnias	8.50	3.00	9.00	3.00	327.50	.341
Sleep-Disordered Breathing	3.00	1.00	3.00	1.00	367.50	.745
Daytime Sleepiness	10.00	5.00	10.50	3.00	380.00	.947
Total CSHQ	43.00	10.00	42.50	7.00	337.50	.440

* Asymptotic significance

Table 51 Mann Whitney U tests of TEA-Ch subtests by gender

	Females (n=32)		Males (n=27)		*U* test	
	Median	*IQR*	Median	*IQR*	*U*	*p**
Sky correct	19.50	1.00	19.00	2.00	400.00	.605
Sky timing	5.03	2.22	5.70	1.90	314.50	.112
Sky attention	3.55	2.18	4.30	1.53	326.00	.159
Score	9.00	3.00	8.00	4.00	393.00	.714
Creature correct	7.00	2.00	6.00	3.00	315.00	.094
Creature timing	4.39	1.19	4.31	1.17	361.50	.668
Sky DT	1.06	3.07	0.70	2.69	381.50	.590
Score DT	16.00	4.00	14.00	6.00	329.50	.236
Same Worlds	28.85	6.94	29.00	4.81	394.50	.737
Opposite Worlds	34.25	9.03	37.00	5.05	314.50	.112

* equal variances not assumed

Table 52 Pearson correlation coefficients of age, actigraphy and CSHQ (n = 56)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Age	1.00																
Actigraphy	-.06	1.00															
Activity index																	
Sleep Duration	**-.43**	-.17	1.00														
Sleep minutes	-.18	**-.65**	**.67**	1.00													
Sleep efficiency	.07	**-.79**	.14	**.79**	1.00												
Long wake episodes	-.12	**.75**	.01	**-.64**	**-.91**	1.00											
Wake after sleep onset	-.13	**.79**	.02	**.70**	**-.99**	**.94**	1.00										
Sleep latency	.11	.08	-.24	-.23	-.16	.12	.15	1.00									
CSHQ	.03	.17	-.23	-.25	-.14	.10	.12	.08	1.00								
Bedtime Resistance																	
Sleep Onset Delay	.02	.07	-.26	-.22	-.03	.04	.02	**.41**	**.40**	1.00							
CSHQ Sleep Duration	.06	.22	-.23	**-.30**	-.17	.19	.15	.11	**.31**	**.54**	1.00						
Sleep Anxiety	-.07	.02	-.10	-.22	-.21	.22	.21	.18	**.60**	**.41**	.15	1.00					
Night Wakings	**-.29**	.04	.09	.03	-.04	.05	.06	.01	**.44**	**.28**	.13	**.49**	1.00				
Parasomnias	-.05	.05	-.22	-.22	-.18	.15	.15	.12	**.35**	**.26**	**.27**	**.36**	**.47**	1.00			
Sleep-Disordered breathing	-.06	.09	-.13	-.14	-.14	.17	.11	**.29**	-.01	.10	.13	-.01	.07	.18	1.00		
Daytime Sleepiness	.02	.05	-.05	-.05	.08	-.08	-.08	.21	.22	**.36**	**.38**	.19	.11	-.03	.14	1.00	
Total CSHQ	.03	.11	-.24	**-.31**	-.18	.15	.16	**.31**	**.69**	**.66**	**.63**	**.64**	**.58**	**.58**	**.26**	**.62**	1.00

Significant correlations, $p < .05$, shown in bold script

Table 53 Pearson correlation coefficients of age, raw TEA-Ch, NEPSY, AWMA scores, & WISC standard Scores (n in brackets)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Age (58)	1.00																		
Sky correct (58)	**.37**	1.00																	
Sky time (57)	**-.49**	-.01	1.00																
Sky attention (57)	**-.34**	-.02	.77	1.00															
Score (57)	**.27**	.15	.01	-.06	1.00														
Creature correct (56)	**.39**	**.34**	**-.31**	**-.28**	.19	1.00													
Creature timing (55)	**-.29**	-.04	**.32**	**.31**	-.12	-.16	1.00												
Sky DT (56)	**-.27**	-.43	.11	.11	-.21	**-.54**	.11	1.00											
Score DT (56)	**.63**	**.32**	**-.45**	**-.28**	**.31**	**.41**	**-.30**	**-.34**	1.00										
Same Worlds (56)	**-.55**	-.06	**.33**	**.26**	**-.37**	**-.32**	.05	.17	**-.37**	1.00									
Opposite Worlds (56)	**-.38**	-.30	.23	.19	-.03	**-.45**	**.32**	**.38**	**-.35**	**.51**	1.00								
Tower (57)	**.27**	-.10	**-.28**	-.25	.00	.13	-.17	-.08	**.31**	-.15	-.13	1.00							
Verbal Fluency (57)	**.56**	.01	**-.52**	-.40	.13	.21	**-.43**	-.22	**.38**	**-.34**	**-.30**	.25	1.00						
Digit Recall (53)	.18	.27	-.18	-.20	.22	.27	-.13	-.23	.14	-.19	**-.28**	-.05	.16	1.00					
Backward Recall (53)	**.30**	-.06	-.22	-.20	-.04	.25	.16	-.12	.24	**-.36**	**-.37**	.23	**.41**	**.37**	1.00				
Spatial Span (52)	**.41**	.03	**-.34**	-.26	.21	**.33**	-.08	-.22	**.46**	**-.28**	**-.36**	.18	**.38**	.23	**.35**	1.00			
Coding (58)	-.21	-.11	**-.39**	-.28	-.06	-.03	.07	.08	-.06	-.19	-.15	.12	.20	.00	**.28**	.15	1.00		
Symbol Search (58)	.03	-.01	**-.37**	**-.31**	.10	**.42**	-.22	**-.32**	**.29**	-.10	-.18	.22	.22	**.30**	**.36**	**.34**	.18	1.00	
Processing speed (58)	.06	.03	**-.53**	**-.41**	.01	**.31**	-.12	-.20	.18	-.19	-.24	.26	**.29**	.22	**.41**	**.32**	**.73**	**.76**	1.00

Significant correlations ($p < .05$) shown in bold

Table 54 Means and *SD* of NEPSY, AWMA, & WISC by gender

	Male			Female			t test	
	n	Mean	*SD*	n	Mean	*SD*	*t*	df	*p*
Tower	27	10.52	2.26	31	11.06	2.05	0.97	56	.339
Verbal Fluency	27	44.00	9.94	32	51.38	18.24	1.85	56	.070
Digit Recall	25	27.08	4.38	29	27.52	3.04	0.43	52	.668
Backward Recall	25	9.88	3.53	29	12.41	4.02	2.44	52	.018
Spatial Span	24	16.12	6.20	29	19.45	4.72	2.22	51	.031
Coding	27	9.63	2.69	32	10.84	2.82	1.68	57	.098
Symbol Search	27	11.37	3.85	32	12.16	2.89	0.90	57	.374
Processing speed	26	102.93	11.59	32	108.47	12.75	1.73	57	.088

Table 55 Mann Whitney U tests of SDQ by gender

	Female (n=31)		Males (n=24)		U test	
	Median	*IQR*	Median	*IQR*	*U*	*p**
Emotional Symptoms	2.00	5.00	1.50	4.00	265.50	.067
Conduct Problems	2.00	3.00	1.00	3.00	368.00	.944
Hyperactivity	4.00	5.00	5.00	3.00	309.00	.282
Peer Problems	1.00	3.00	1.50	4.00	322.50	.383
Pro-social	9.00	3.00	9.00	3.00	321.00	.370
Total SDQ	9.00	12.00	10.50	6.00	334.50	.524

*Asymptotic significance

Table 56 Means and *SD* of BRIEF scores in high and low sleep disturbance groups

	Low sleep disturbance (n=25)		High sleep disturbance (n=27)	
	Mean	*SD*	Mean	*SD*
Inhibit	50.59	9.68	54.93	9.89
Shift	51.22	10.58	53.11	10.84
Emotional Control	53.33	10.01	54.52	10.67
Initiate	54.96	10.87	52.41	9.49
Working Memory	54.56	13.01	56.52	10.71
Plan/Organize	52.81	10.24	56.15	11.78
Organisation of Materials	54.04	10.55	52.15	10.78
Monitor	51.56	9.07	53.26	9.95
Behavioural Regulation	51.48	10.17	54.70	10.03
Metacognition	54.52	10.10	55.04	10.83
Total BRIEF	53.73	9.32	55.38	10.38

Table 57 Pearson correlation coefficients of actigraphy (n = 56) and BRIEF (n = 57) scores

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Sleep duration	1.00																	
Sleep minutes	**.64**	1.00																
Sleep efficiency	.11	**.78**	1.00															
Long wake episodes	.04	**-.64**	**-.91**	1.00														
Wake after sleep onset	.03	**-.70**	**-.99**	**.94**	1.00													
Sleep latency	-.21	-.20	-.15	.11	.14	1.00												
Activity index	-.15	**-.65**	**-.79**	**.75**	**.78**	.07	1.00											
Inhibit	-.19	-.22	-.04	.01	.00	-.10	.06	1.00										
Shift	-.18	-.17	-.10	.10	.08	.02	.14	**.43**	1.00									
Emotional Control	-.02	-.12	-.11	.09	.11	-.03	.11	**.48**	**.52**	1.00								
Initiate	**-.34**	-.06	.23	-.25	-.27	.12	-.05	**.41**	**.56**	**.40**	1.00							
Working Memory	**-.27**	-.21	-.05	.04	.01	.17	.12	**.43**	**.69**	**.37**	**.67**	1.00						
Plan/Organize	**-.35**	**-.29**	-.08	.04	.03	.17	.20	**.43**	**.67**	**.37**	**.72**	**.75**	1.00					
Organisation of Materials	**-.35**	-.18	.07	-.11	-.12	.09	.01	**.34**	**.31**	**.39**	**.49**	**.43**	**.56**	1.00				
Monitor	-.12	-.10	.04	-.07	-.07	-.01	.08	**.71**	**.61**	**.59**	**.69**	**.63**	**.68**	**.37**	1.00			
Behavioural Regulation	-.19	-.20	-.13	.13	.10	-.03	.18	**.81**	**.72**	**.81**	**.57**	**.59**	**.58**	**.40**	**.76**	1.00		
Metacognition	**-.31**	-.21	.04	-.01	-.09	.12	.03	**.52**	**.67**	**.46**	**.85**	**.77**	**.88**	**.65**	**.74**	**.66**	1.00	
GEC (total BRIEF)	**-.31**	-.24	-.04	.00	-.01	.09	.13	**.70**	**.75**	**.67**	**.82**	**.79**	**-.85**	**.65**	**.84**	**.85**	**.91**	1.00

Significant correlations, $p < .05$, shown in bold script

Table 58 Pearson correlation coefficients between CSHQ (n = 56) and BRIEF (n = 57)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Bedtime Resistance	1.00																			
Sleep Onset Delay	**.40**	1.00																		
Sleep Duration	**.29**	**.53**	1.00																	
Sleep Anxiety	**.59**	**.38**	.12	1.00																
Night Wakings	**.46**	**.30**	.16	**.51**	1.00															
Parasomnias	**.36**	**.28**	**.28**	**.37**	**.50**	1.00														
Sleep-Disordered Breathing	-.04	.12	.13	-.01	.08	.18	1.00													
Daytime Sleepiness	.23	**.31**	**.34**	.16	.15	-.03	.20	1.00												
Total CSHQ	**.70**	**.64**	**.62**	**.64**	**.64**	**.60**	**.28**	**.60**	1.00											
Inhibit	**.37**	.25	**.31**	.04	**.27**	.16	.20	**.34**	**.42**	1.00										
Shift	**.32**	.21	**.41**	.19	.08	.07	.12	**.35**	**.38**	**.44**	1.00									
Emotional Control	**.42**	**.36**	**.46**	.23	.20	.19	.23	**.57**	**.59**	**.49**	**.52**	1.00								
Initiate	.23	**.34**	.22	-.10	-.08	.01	.10	**.36**	.26	**.37**	**.56**	**.40**	1.00							
Working Memory	.24	**.42**	**.43**	.00	.07	.06	.14	**.39**	**.38**	**.38**	**.41**	**.37**	**.67**	1.00						
Plan/organize	**.29**	**.35**	**.38**	-.06	-.07	-.03	.00	**.38**	**.32**	**.40**	**.67**	**.37**	**.72**	**.75**	1.00					
Org. of Materials	.19	**.37**	**.26**	-.07	-.26	-.20	.03	**.28**	.13	**.34**	**.31**	**.39**	**.49**	**.43**	**.56**	1.00				
Monitor	.22	**.31**	**.36**	-.15	.10	.05	.20	**.38**	**.32**	**.71**	**.61**	**.59**	**.69**	**.63**	**.68**	**.37**	1.00			
Behavioural Regulation	**.47**	**.35**	**.44**	.18	**.27**	.19	**.24**	**.42**	**.54**	**.81**	**.72**	**.81**	**.57**	**.59**	**.58**	**.40**	**.76**	1.00		
Metacognition	**.27**	**.40**	**.36**	-.04	-.07	-.05	.10	**.52**	**.38**	**.52**	**.67**	**.46**	**.85**	**.77**	**.88**	**.65**	**.74**	**.66**	1.00	
Total BRIEF	**.38**	**.43**	**.45**	.05	.06	.08	.18	**.51**	**.48**	**.70**	**.75**	**.67**	**.82**	**.79**	**.85**	**.65**	**.84**	**.85**	**.91**	1.00

Significant correlations, $p < .05$, shown in bold script

Table 59 Pearson correlation coefficients of SDQ (n = 55) and BRIEF (n = 57)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Emotional Symptoms	1.00																
Conduct Problems	**.31**	1.00															
Hyperactivity	**.31**	**.55**	1.00														
Peer Problems	.16	.12	.12	1.00													
Pro-Social Scale	.06	**-.52**	-.14	-.01	1.00												
Total SDQ	**.59**	**.63**	**.82**	**.44**	-.12	1.00											
Inhibit	.04	**.57**	**.53**	**.34**	**-.28**	**.56**	1.00										
Shift	**.42**	**.42**	**.47**	**.38**	**-.29**	**.58**	**.44**	1.00									
Emotional Control	**.50**	**.60**	**.39**	.23	**-.42**	**.58**	**.49**	**.57**	1.00								
Initiate	**.27**	.24	**.44**	**.49**	**-.29**	**.53**	**.37**	**.58**	**.43**	1.00							
Working Memory	**.36**	**.53**	**.59**	**.37**	**-.30**	**.62**	**.41**	**.70**	**.41**	**.69**	1.00						
Plan/Organize	.25	**.49**	**.61**	**.41**	**-.32**	**.58**	**.40**	**.68**	**.40**	**.75**	**.77**	1.00					
Org. Materials	.02	**.34**	**.35**	.19	**-.31**	.25	**.34**	**.31**	**.39**	**.47**	**.43**	**.56**	1.00				
Monitor	.22	**.52**	**.49**	**.33**	**-.44**	**.56**	**.65**	**.61**	**.59**	**.71**	**.65**	**.68**	**.37**	1.00			
Behavioural Regulation	**.40**	**.64**	**.55**	**.39**	**-.39**	**.69**	**.81**	**.74**	**.82**	**.56**	**.59**	**.58**	**.40**	**.76**	1.00		
Metacognition	**.29**	**.48**	**.56**	**.43**	**-.37**	**.60**	**.48**	**.68**	**.48**	**.86**	**.79**	**.88**	**.65**	**.74**	**.66**	1.00	
Total BRIEF	**.32**	**.60**	**.63**	**.47**	**-.42**	**.69**	**.68**	**.77**	**.70**	**.82**	**.80**	**.85**	**.65**	**.84**	**.85**	**.91**	1.00

Significant correlations, $p < .05$, shown in bold script

Appendix C. Study 3 Additional Information

Appendix C.1. NHS Ethics Approval

MFK

ISLE OF WIGHT, PORTSMOUTH & SOUTH EAST HAMPSHIRE RESEARCH ETHICS COMMITTEE

1ST Floor, Regents Park Surgery
Park Street, Shirley
Southampton
Hampshire
SO16 4RJ

Tel: 023 8036 2863
Fax: 023 8036 4110

Email: scsha.SEHREC@nhs.net

27 March 2008

Mrs Simone Holley
Postgraduate Student
Department of Psychology
University of Southampton
Highfield, Southampton
SO17 1BJ

Dear Mrs Holley

Full title of study: **Sleep quality, night-time respiratory function, and neuropsychological functioning in children with cystic fibrosis**

REC reference number: **08/H0501/26**

The Research Ethics Committee reviewed the above application at the meeting held on 14 March 2008. Thank you for attending to discuss the study.

Documents reviewed

The documents reviewed at the meeting were:

Document	*Version*	*Date*
Application	IRAS	18 February 2008
Investigator CV		18 February 2008
Protocol	1	04 February 2008
Covering Letter		20 February 2008
Letter from Sponsor		11 February 2008
Peer Review		08 February 2008
Compensation Arrangements		11 February 2008
Questionnaire: Additional Information - non-validated	1	18 February 2008
Questionnaire: SDQ - Validated		
Questionnaire: Sleep Self Report - Validated		
Questionnaire: CSHQ - Validated		
Questionnaire: Brief - Validated		
Participant Information Sheet: Child Sleep Lab	1	18 February 2008
Participant Information Sheet: Parent Sleep Lab	1	18 February 2008
Participant Information Sheet: Child	1	18 February 2008
Participant Information Sheet: Parents	1	18 February 2008
Participant Consent Form: Child Sleep Lab	1	18 February 2008
Participant Consent Form: Parent Sleep Lab	1	18 February 2008
Participant Consent Form: Child	1	25 January 2008
Participant Consent Form: Parent	1	18 February 2008
Supervisor's CV		

Provisional opinion

The Committee would be content to give a favourable ethical opinion of the research, subject to receiving a complete response to the request for further information set out below.

The Committee delegated authority to confirm its final opinion on the application to the Chair.

Further information or clarification required

i) √ Please add the Researcher's department postal address to the 'header' of the PIS. 1-2
ii) Please correct the name for the Research Ethics Committee on the PIS to IOW, Portsmouth and South East Hampshire REC.
iii) Please give an answer to the question 'Why have I been chosen?' on the PIS
iv) The Committee would like the Researcher to note that lone-worker policy should have a reporting back mechanism e.g. when the lone-worker leaves the visiting premises, please provide this.
v) Please remove the phrase 'will I have fun' from the child's PIS

The Committee would like to congratulate the Researcher for their effort in trying to obtain informed consent from the child participant.

When submitting your response to the Committee, please send revised documentation where appropriate underlining or otherwise highlighting the changes you have made and giving revised version numbers and dates.

The Committee will confirm the final ethical opinion within a maximum of 60 days from the date of initial receipt of the application, excluding the time taken by you to respond fully to the above points. A response should be submitted by no later than 25 July 2008.

Ethical review of research sites

The Committee agreed that all sites in this study should be exempt from site-specific assessment (SSA). There is no need to submit the Site-Specific Information Form to any Research Ethics Committee. However, all researchers and local research collaborators who intend to participate in this study at NHS sites should seek approval from the R&D office for the relevant care organisation.

Membership of the Committee

The members of the Committee who were present at the meeting are listed on the attached sheet.

Richard Thwaites stated that his department had professional links with the study team. After a brief discussion it was agreed that there was not conflict of interest and Richard Thwaites took a full part in the review.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

08/H0501/26	Please quote this number on all correspondence

Yours sincerely

p/p **Mr David Carpenter**
Chair

Email: scsha.SEHREC@nhs.net

Enclosures: List of names and professions of members who were present at the meeting.

Copy to: Ms Angela Jackson, Research Governance Officer, SUHT

School of Psychology, University of Southampton
Highfield, Southampton, SO17 1BJ
Tel: 02380 594593
Email: slh604@soton.ac.uk

UNIVERSITY OF Southampton
School of Psychology
School of Medicine

Sleep, Learning, & Behaviour in Children with Cystic Fibrosis
Participant information sheet for parents

We would like to invite you and your child to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it would involve. Please read the following information carefully and discuss it with others if you wish. Take time to decide if you want your child to take part. If anything is unclear, or if you need to know more, please ask.

Who is running the study?
Mrs Simone Holley, PhD research student, School of Psychology, University of Southampton
Dr Catherine Hill, Senior Lecturer in Child Health, School of Medicine, University of Southampton
Drs Gary Connett and Julian Legg, Consultant Respiratory Paediatricians, Southampton University Hospitals NHS Trust
Professor Jim Stevenson, School of Psychology, University of Southampton

What is the purpose of the study?
Previous research has shown that children with cystic fibrosis (CF) can have sleep disturbance caused by night-time symptoms. Previous research has also shown that sleep disturbance can affect attention and other brain functions in normal, healthy children. The study aims to examine whether children with CF have greater sleep disturbance compared with healthy children. We are also interested in whether children with CF have specific problems with attention, memory, and behaviour that may be caused by sleep disturbance. This project forms part of a PhD thesis being conducted by Simone Holley, a PhD student in the School of Psychology.

Why has my child been chosen?
Your child has been chosen because he or she is under the care of a consultant who has been asked to find suitable children for this study. The study should have been explained to you by your child's consultant or CF nurse, who should have asked for your permission to be contacted by the lead researcher for this project. We need to recruit 40 children with cystic fibrosis aged between 6 and 13 years of age. To take part, your child must **not** have any of the following:

- Any statement of special educational needs (SEN) for learning difficulties
- Any visual or motor disabilities that may impair their physical ability to participate in attention and memory testing
- Children must not have any respiratory infection at the time of testing

Do we have to take part?

You and your child's participation is voluntary, it is up to you to decide whether or not you wish to take part, but we would ask that you ensure your child understands what is involved and is willing to take part. If you agree to take part, you will be asked to sign a consent form but you should be aware that even though you sign the consent form, you are still free to withdraw your child from the study at any time without giving reason. This would not affect the standard of care you receive.

What will happen to my child if they take part?

The study will last for 1 week and all assessments will take place in your home. The study involves your child wearing an actigraph, a small, lightweight, watch-like device that will need to be worn on the wrist for 7 consecutive days and nights. This device measures movement and enables us to examine the amount of disruption to your child's sleep. It can be taken off to bath/shower and for any other activities where necessary. During two nights of the actigraphy recording, your child would also have their blood oxygen saturation measured using a pulse oximeter. This device involves wearing a sensor on the fingertip throughout the night. At the end of the 7 days of actigraphy, a researcher will conduct some psychological tests with your child that test attention, memory, and other aspects of learning. Some of these will be paper and pencil tests, and some will be computer based. Unfortunately, we will not be able to provide any feedback on the day about your child's performance on the psychological tasks. However, we will send you a brief description of your child's performance on these measures throughout the study after the final visit. This will give you an idea about how they performed compared to other children, but will not be a detailed psychology report. However, if you are concerned about your child's performance you may contact us and we can advise you how to enquire about a more formal assessment.

1st Visit

Simone will come to your home and ensure that you and your child fully understand the project. She will explain the equipment used in the study and describe the psychology tests that would be carried out. Simone will answer any questions you or your child have about the study. If you remain interested to take part, Simone will ask you and your child to sign a consent form, these forms are used to ensure you fully understand about the project – they do not commit you to taking part. A questionnaire pack will be left with you for you to complete at your leisure. The first visit will last approximately 20 minutes.

2nd Visit

At the end of the 7 days of actigraphy, Simone will return at a convenient time (not during school time) to conduct the psychology tests. These will need to be conducted in a quiet room with a table and chair. It is preferable that you are not in the same room whilst the tests are being conducted, however if you would prefer to be present then you may watch. The psychology tests will take no more than 1 hour and 45 minutes.

Follow-up

After this study, we will also be inviting some children to take part in a subsequent phase of the project. This would involve spending one night in the special sleep centre at the Wellcome Trust Clinical Research Facility at Southampton General Hospital. After we have looked at the actigraphy sleep data we will contact children who had the least and the greatest amount of sleep disturbance. We will only contact you if you agree to this on the consent form. If we do contact you, you will be given full details of the sleep centre study before you agree to take part. Any travelling costs incurred if you take part in the second phase will be reimbursed.

What do I have to do?

During the home based study, you would need to record the time your child went to bed and got up in the morning. There are also some questionnaires for you to complete about your child's sleep and behaviour. There is also a questionnaire that includes personal questions about you and your partner's (where applicable) employment and educational background. Please note that you are under no obligation to provide answers to any of the questions. In total, the questionnaires would take about 30 minutes to complete.

What are the possible disadvantages and side-effects (risks) to my child if he / she takes part?

This study will not administer any treatments (medicines) and the procedures are unlikely to cause any harm or discomfort. In the unlikely event that you or your child finds any part of the study upsetting, you will have an opportunity to discuss your concerns with the researchers. The actigraph has been successfully used in previous studies with children. Very occasionally, a child may be resistant to wearing the watch and find it uncomfortable. Similarly, some children may find the oximeter uncomfortable. In these instances, you can withdraw your child from the study.

What are the possible benefits of taking part?

We hope that you will find participating in this study an enjoyable experience. The information obtained from the oximeter will provide you child's doctor with information on your child's oxygen levels while asleep that may be relevant to their condition. At the end of the study, you will be given a summary sheet of what the actigraph records about your child's sleep, and summary information from the psychological tests. Many children often find wearing the actigraph fun and the psychological tests enjoyable.

What happens when the research study finishes?

The information obtained from your child and the other children will be put together and carefully analysed. (Please note that all information obtained from children and families will be coded and remain anonymous.) Our findings will be reported in research articles and conferences in the UK and overseas. This will enable other doctors to learn from our study.

What if something goes wrong?

If you are concerned about any part of the study we advise you in the first instance to talk to the researchers (telephone number at the top). If you would like to take your concerns further you may speak to your ENT doctor and/or ask your doctor about the standard hospital complaints procedure.

Will the information obtained be confidential?

If you consent to take part in the study, your child's medical records will be accessed by the health professionals in the study. All information about your child that is collected during the course of the study will be kept strictly confidential. The results of your child's sleep study will only be sent to his / her CF doctor, and the psychology results will only be sent to you. Results of this study will not include your or your child's name, or any other identifying characteristics. Procedures for handling, processing, storage and destruction of data is compliant with the Data Protection Act 1998. Data will be stored anonymously and securely on disc for up to 15 years and then disposed of securely. Only authorised persons will have access to the data.

Who is organising and funding the research?

This study is being organised by those researchers whose names are listed at the top. A charitable Trust (Gerald Kerkut Charitable Trust) is providing the funding for the PhD research.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee (REC) to protect your safety, rights, wellbeing, and dignity. This study has been reviewed and given favourable opinion by the IOW, Portsmouth, and South East Hampshire REC. This study has also been reviewed by the University of Southampton, School of Psychology Research Ethics Committee.

Complaints

If you have a concern about any aspect of this study or you wish to make a complaint, you may contact the Chair of the Ethics Committee, Department of Psychology, University of Southampton, Southampton, SO17 1BJ. Phone: (023) 8059 5578.

Contact for further information

If you have further questions please contact Simone Holley, at the University of Southampton on 02380594593, or email slh604@soton.ac.uk. Alternatively you may contact Dr Cathy Hill on xxxxxxxxxxxxxxx

Thank you for your time!

School of Psychology, University of Southampton
Highfield, Southampton, SO17 1BJ
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UNIVERSITY OF Southampton
School of Psychology
School of Medicine

Sleep, Learning, & Behaviour in Children with Cystic Fibrosis
Information sheet for child

We are asking if you would like to take part in a research project to find out if your CF affects your sleep during the night. We are also trying to find out if children are better at learning when they sleep well. Before you decide to take part, it is important that you understand why the research is being done and what will happen to you. Please read this leaflet carefully and ask your mum or dad anything you do not understand.

What is research? Why is this project being done?
Research is way we try to find out the answers to questions. We want to find out if children with CF have trouble sleeping because of their illness. We also want to know if sleeping badly affects how well children can learn, pay attention, and remember things.

Why have I been asked to take part?
You have been invited to join our study because you have CF and doctor is involved in the study. 40 children who have CF aged between 6 and 13 years will be invited to take part. 40 children who do not have CF have already taken part in this project.

Did anyone else check the study is OK to do?
Before any research is allowed to happen, it has to be checked by a group of people called a Research Ethics Committee. They make sure the research is fair. You project has been checked by the Isle of Wight, Portsmouth, and South East Hampshire Research Ethics Committee.

Do I have to take part?
No! It is up to YOU. You must only take part if you want to, and if your parents are happy for you to take part. If you do agree to take part you will be asked to sign (write your name) a form saying that you are happy to take part. You are free to stop taking part at any time during the research without giving a reason. If you decide to stop taking part it will not affect the care you receive.

What will happen to me if I take part?
A researcher will come to your house, explain the project to you and show you the equipment that will be used. If you decide to take part, you will be asked to wear a special watch (called an actigraph) for seven days and nights. This will tell me how much you move around when you are sleeping. You will also be asked to wear a large plaster on your fingertip for two nights that is connected to a small machine. This tells me how much oxygen is in your blood. At the end of the seven days a

researcher will come to your house to do some special tasks with you, these will take about 1 hour and 45 minutes. Some children find these tests enjoyable. The tests are not like literacy or numeracy tests that you do at school. Some tests ask you to listen carefully at sounds on a computer, some ask you to remember numbers. Another test asks you to make patterns with coloured wooden balls. You will also be asked to answer some questions about your sleep. Your parents will answer some questions about your sleep and behaviour.

Is there anything for me to be worried about?
A few children sometimes find the watch a little uncomfortable especially if you are not used to wearing a watch. Also, you may find the finger sensor uncomfortable but it will not hurt. Remember, you can say at anytime if you want to stop taking part, either when you are wearing the watch or doing the tasks. You will not get into trouble if you decide to stop.

Will my medical details be kept private if I take part? Will anyone else know I'm doing this?
Only the researchers involved in the project and your doctors will know you are taking part.

If you have any questions or there is anything you don't understand you can ask the researcher who comes to your home or your parents.

UNIVERSITY OF Southampton
School of Psychology
School of Medicine

Impact of Sleep Quality on Daytime Functioning in Children with Epilepsy

Parent consent form

Please initial boxes

1. I confirm that I have read and understood the information sheet dated ……. for the above study (version……). I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily. ☐
2. I understand that my child's participation is voluntary and that I am free to withdraw my child at any time, without giving any reason, without my child's medical care or legal rights being affected. ☐
3. I give permission for the researchers involved in the project to have access to my child's medical records. ☐
4. I agree to allow the named researchers to store anonymized results obtained from my child on a CD disc/Hospital or University computer for up to 15 years after the study. ☐
5. I understand that I will need to complete questionnaires about my child for the study ☐
6. I agree to let my child take part in the above study. ☐
7. The study has been described to my child. I am satisfied that he/she is happy to take part. I understand that I may withdraw them from the study at any time if I believe they are unhappy. ☐

_____	_____	_____
Name of parent	Date	Parent's Signature
_____	_____	_____
Researcher	Date	Signature

UNIVERSITY OF Southampton
School of Psychology
School of Medicine

Sleep, Learning, & Behaviour in Children with Cystic Fibrosis
Consent form for child

Have you read (or had read to you) about this project?	Yes/No
Has somebody else explained this project to you?	Yes/No
Do you understand what this project is about?	Yes/No
Have you asked all the questions you want?	Yes/No
If you asked any questions- Have they been answered in a way you understand?	Yes/No
Do you understand it's OK to stop taking part at any time?	Yes/No
Are you happy to take part?	Yes/No

If any answers are 'no' or you **don't** want to take part, **don't** sign your name!

If you do want to take part, please write your name and today's date

Your name _____

Date _____

Name of Researcher: Simone Holley

Signature: _____

Table 60 Kolmogorov-Smirnov tests of main variables for CF sample

	D	df	*p*
Sleep duration	.145	25	.186
Total sleep minutes	.155	25	.125
Sleep efficiency	.129	25	.200*
Sleep latency	.120	25	.200*
Long wake episodes	.133	25	.200*
Activity index	.122	25	.200*
Wake after sleep onset	.095	25	.200*
Child Sleep Habits Questionnaire total	.117	24	.200*
Strengths & Difficulties total score	.100	25	.200*
BRIEF total score	.162	25	.089
Processing Speed	.133	25	.200*
Global Executive Function Score	.127	25	.200*

* This is a lower bound of the true significance.

Table 61 CF children actigraphy sleep variables means and *SD* by gender

	Males (n=12)		Females (n=13)		t test (df = 23)	
	Mean	*SD*	Mean	*SD*	*t*	*p*
Sleep duration	556.12	29.88	570.14	35.86	1.057	.302
Total sleep minutes	462.77	44.03	483.31	60.78	0.960	.347
Sleep efficiency	83.62	8.06	85.54	9.44	0.544	.594
Sleep latency	39.56	19.64	44.99	21.41	0.659	.517
Long wake episodes	5.23	2.44	4.43	2.87	-0.750	.461
Activity index	49.90	16.19	41.31	13.78	-1.432	.166
Wake after sleep onset	90.97	43.86	81.92	52.94	-0.464	.647

Table 62 Mann Whitney U tests of CSHQ by gender in children with CF

	Females (n=13)		Males (n=12)		U test	
	Median	*IQR*	Median	*IQR*	*U*	*p**
Bedtime Resistance	7.00	1.00	6.00	1.00	57.50	.424
Sleep Onset Delay	1.00	2.00	2.00	1.00	59.00	.494
Sleep Duration	3.00	2.00	3.00	2.00	64.00	.691
Sleep Anxiety	4.00	3.00	4.00	1.00	61.00	.569
Night Wakings	4.00	2.00	3.00	0.00	26.00	.007
Parasomnias	9.00	2.00	8.00	2.00	58.00	.459
Sleep-disordered breathing	3.00	1.00	3.00	1.00	69.00	.910
Daytime Sleepiness	15.00	5.00	13.00	5.00	33.50	.026
Total CSHQ	47.00	7.00	41.00	10.00	43.00	.106

*Exact significance

Table 63 Mann Whitney U tests of SDQ by gender in children with CF

	Female (n=13)		Males (n=12)		U test	
	Mean	*IQR*	Mean	*IQR*	*U*	*p**
Emotional Symptoms	3.00	3.00	2.00	1.00	52.00	.168
Conduct Problems	1.00	2.00	1.00	2.00	59.50	.320
Hyperactivity	3.00	4.00	4.00	2.00	77.50	.979
Peer Problems	2.00	4.00	1.00	3.00	71.50	.728
Pro-social	9.00	4.00	9.00	3.00	68.00	.611
Total SDQ	11.00	9.00	7.00	7.00	57.00	.270

*Exact significance

Table 64 Pearson correlation coefficients of age, actigraphy, and CSHQ in CF children (n = 25)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Age	1.00																
Activity index	-.15	1.00															
Sleep duration	**-.61**	.10	1.00														
Sleep minutes	-.21	**-.71**	**.45**	1.00													
Sleep efficiency	.05	**-.87**	-.04	.85	1.00												
Long wake episodes	-.17	**.89**	.26	**-.66**	**-.91**	1.00											
Wake after sleep onset	-.09	**.87**	.14	**-.79**	**-.99**	**.94**	1.00										
Sleep latency	-.12	.30	-.19	-.36	-.30	.20	.28	1.00									
Bedtime Resistance	-.06	-.25	-.31	.13	.28	-.37	-.31	.06	1.00								
Sleep Onset Delay	-.31	.08	-.11	-.08	-.06	.07	.04	**.73**	.18	1.00							
CSHQ Sleep Duration	**-.42**	.21	.05	-.23	-.29	.15	.26	.31	-.04	.36	1.00						
Sleep Anxiety	-.35	-.19	**.42**	**.42**	.23	-.22	-.21	-.30	.24	-.08	.17	1.00					
Night Wakings	.05	-.28	-.13	.15	.17	-.27	-.20	.03	.37	.09	-.06	.25	1.00				
Parasomnias	-.05	.19	.00	-.07	-.14	.19	.14	.16	.19	.15	.19	.04	.26	1.00			
Sleep-disordered Breathing	.24	.12	-.17	-.20	-.17	.12	.15	.04	.10	-.09	.24	.13	-.08	**.55**	1.00		
Daytime Sleepiness	.23	.20	-.21	-.34	-.34	.19	.31	**.43**	.13	.11	.29	.02	**.49**	**.47**	**.43**	1.00	
Total CSHQ	-.08	.10	-.12	-.15	-.18	.06	.15	.39	.41	.33	**.52**	.31	**.54**	**.67**	**.52**	**.83**	1.00

Significant correlations, $p < .05$, shown in bold script

Table 65 Mann Whitney U tests of TEA-Ch subtests by gender in children with CF

	Females (n=13)		Males (n=12)		U test	
	Median	*IQR*	Median	*IQR*	*U*	*p**
Sky correct	20.00	1.00	19.50	2.00	71.00	.728
Sky timing	5.35	1.94	4.59	4.16	68.00	.611
Sky attention	3.90	1.74	3.66	4.21	66.50	.538
Score	8.00	3.00	10.00	3.00	60.00	.347
Creature correct	6.00	2.00	6.00	3.00	71.50	.728
Creature timing	3.75	2.40	3.88	3.51	75.50	.894
Sky DT	0.25	4.10	0.37	2.03	69.50	.650
Score DT	17.00	5.00	16.50	7.00	72.00	.769
Same Worlds	28.80	9.85	26.65	15.33	76.50	.936
Opposite Worlds	36.80	11.30	31.95	18.55	71.00	.728

*Exact significance

Table 66 Means and *SD* of NEPSY, AWMA, & WISC by gender in children with CF

	Male (n=12)		Female (n=13)		t test (df = 23)	
	Mean	*SD*	Mean	*SD*	*t*	*p*
Tower	10.50	1.78	10.62	2.57	0.129	.898
Verbal Fluency	50.75	15.14	50.15	12.65	-0.107	.916
Digit Recall	29.54	4.81	27.00	3.92	-1.476	.153
Backward Digit Recall	13.62	4.63	11.54	5.11	-1.086	.288
Spatial Span	18.00	5.18	17.38	3.73	-0.348	.731
Coding	9.5	2.97	11.08	3.20	1.274	.215
Symbol Search	12.25	2.38	12.69	3.95	0.336	.740
Processing speed	105.00	13.07	110.46	15.85	0.935	.359

Table 67 Pearson correlation coefficients of age, raw TEA-Ch, NEPSY, AWMA scores, & WISC standard scores in CF children (n=25)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Age	1.00																		
Sky correct	.13	1.00																	
Sky time	**-.68**	-.30	1.00																
Sky attention	**-.50**	-.15	**.76**	1.00															
Score	**.41**	.06	-.17	.01	1.00														
Creature correct	**.46**	.07	-.28	-.07	.21	1.00													
Creature timing	**-.58**	-.26	**.78**	**.50**	-.12	-.18	1.00												
Sky DT	**-.51**	.02	.10	-.01	-.16	**-.82**	.10	1.00											
Score DT	**.65**	.37	**-.69**	**-.48**	**.48**	.36	**-.51**	-.17	1.00										
Same Worlds	**-.69**	-.31	**.81**	**.47**	-.38	**-.46**	**.73**	.29	**-.65**	1.00									
Opposite Worlds	**-.74**	-.18	**.80**	**.49**	**-.44**	**-.58**	**.66**	.36	**-.68**	**.95**	1.00								
Tower	.34	**.40**	-.26	-.16	.28	-.01	-.28	-.03	.30	-.32	-.26	1.00							
Verbal Fluency	**.62**	.20	**-.41**	**-.41**	**.40**	.09	-.29	-.20	**.62**	**-.54**	**-.50**	.27	1.00						
Digit Recall	.33	.00	-.12	-.06	.32	.06	-.22	-.30	.33	-.16	-.21	.12	.37	1.00					
Backward recall	**.56**	.12	-.33	-.09	**.69**	.33	-.33	-.39	**.54**	**-.40**	**-.45**	.17	**.49**	**.40**	1.00				
Spatial Span	**.44**	.16	**-.49**	-.14	**.53**	.31	**-.55**	-.09	**.50**	**-.54**	**-.62**	.18	.18	.29	**.51**	1.00			
Coding	-.12	-.12	-.13	-.20	-.12	-.31	-.15	.29	-.19	-.19	-.13	.20	.07	-.38	-.08	-.10	1.00		
Symbol Search	-.05	.09	-.31	-.39	.08	.17	-.09	-.08	.08	-.29	-.33	-.11	-.11	-.09	-.06	.11	.33	1.00	
Processing Speed	-.11	-.02	-.27	-.35	-.03	-.10	-.15	.13	-.08	-.30	-.28	.06	-.02	-.29	-.09	.00	**.81**	**.81**	1.00

Significant correlations, $p < .05$, shown in bold script

Table 68 Pearson correlation coefficients of actigraphy and BRIEF scores in children with CF (n = 25)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Sleep duration	1.00																	
Sleep minutes	**.47**	1.00																
Sleep efficiency	-.05	**.83**	1.00															
Long wake episodes	.29	**-.62**	**-.90**	1.00														
Wake after sleep onset	.15	**-.78**	**-.99**	**.93**	1.00													
Sleep latency	-.10	-.32	-.30	.23	.28	1.00												
Activity index	.12	**-.69**	**-.86**	**.88**	**.89**	.31	1.00											
Inhibit	.10	-.38	**-.52**	.39	**.51**	.15	.28	1.00										
Shift	.02	-.13	-.20	.00	.19	.01	.01	**.65**	1.00									
Emotional Control	.04	-.34	**-.45**	.31	**.46**	.16	.25	**.78**	**.71**	1.00								
Initiate	.00	**-.40**	**-.51**	.36	**.49**	.31	**.40**	**.73**	**.64**	**.66**	1.00							
Working Memory	.05	-.36	**-.49**	.36	**.49**	.15	.29	**.81**	**.74**	**.75**	**.75**	1.00						
Plan/Organize	.02	-.25	-.35	.23	.35	.34	.20	**.64**	**.75**	**.68**	**.79**	**.78**	1.00					
Org. Materials	-.37	-.27	-.12	.11	.09	.04	.09	.27	.14	.18	.39	.37	.33	1.00				
Monitor	-.03	-.37	**-.44**	.28	**.41**	**.53**	.30	**.67**	**.60**	**.71**	**.80**	**.63**	**.78**	.13	1.00			
Behavioural Regulation	.07	-.33	**-.46**	.29	**.46**	.15	.23	**.91**	**.85**	**.93**	**.76**	**.86**	**.77**	.23	**.74**	1.00		
Metacognition	.00	-.35	-.37	.23	.36	.32	.22	**.75**	**.71**	**.69**	**.84**	**.81**	**.87**	**.44**	**.77**	**.80**	1.00	
GEC (total BRIEF)	.01	-.37	**-.48**	.33	**.47**	.26	.29	**.87**	**.81**	**.85**	**.88**	**.91**	**.90**	**.40**	**.82**	**.94**	**.91**	1.00

Significant correlations, $p < .05$, shown in bold script

Table 69 Pearson correlation coefficients between CSHQ and BRIEF scores in children with CF (n = 24)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Bedtime Resistance	1.00																			
Sleep Onset Delay	.18	1.00																		
Sleep Duration	-.04	.36	1.00																	
Sleep Anxiety	.24	-.08	.17	1.00																
Night Wakings	.37	.09	-.06	.25	1.00															
Parasomnias	.19	.15	.19	.04	.26	1.00														
Sleep-Disordered Breathing	.10	-.09	.24	.13	-.08	**.55**	1.00													
Daytime Sleepiness	.13	.11	.29	.02	**.49**	**.47**	**.43**	1.00												
Total CSHQ	**.41**	.33	**.52**	.31	**.54**	**.67**	**.52**	**.83**	1.00											
Inhibit	-.16	.18	**.42**	.03	.35	.38	.19	**.52**	**.52**	1.00										
Shift	.15	.04	.33	.40	.34	.31	.25	**.53**	**.58**	**.68**	1.00									
Emotional Control	-.09	.02	**.46**	.06	.22	.36	.33	**.70**	**.61**	**.80**	**.71**	1.00								
Initiate	-.01	.28	**.56**	.11	.24	**.51**	.18	**.64**	**.69**	**.73**	**.66**	**.66**	1.00							
Working Memory	-.06	.07	.40	.24	.32	**.44**	**.41**	**.71**	**.68**	**.81**	**.77**	**.76**	**.75**	1.00						
Plan/Organize	-.07	.27	**.42**	.16	.08	**.49**	.30	**.61**	**.61**	**.64**	**.77**	**.69**	**.79**	**.78**	1.00					
Org. Materials	.40	.25	.14	.08	.28	.37	.21	.38	**.50**	.27	.14	.18	.39	.37	.33	1.00				
Monitor	-.07	.39	**.61**	-.04	.10	**.42**	.29	**.64**	**.66**	**.66**	**.63**	**.73**	**.81**	**.63**	**.78**	.13	1.00			
Behavioural Regulation	-.05	.10	**.46**	.16	.33	.40	.29	**.65**	**.64**	**.92**	**.86**	**.93**	**.76**	**.87**	**.78**	.23	**.75**	1.00		
Metacognition	-.05	.24	**.52**	.18	.17	**.47**	.30	**.61**	**.65**	**.75**	**.74**	**.71**	**.84**	**.81**	**.87**	**.44**	**.77**	**.81**	1.00	
GEC (total BRIEF)	-.02	.23	**.52**	.17	.28	**.49**	.32	**.71**	**.73**	**.87**	**.83**	**.87**	**.88**	**.91**	**.90**	**.40**	**.83**	**.95**	**.91**	1.00

Significant correlations, $p < .05$, shown in bold script

Table 70 Pearson correlation coefficients of SDQ (n = 55) and BRIEF (n = 57)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Emotional Symptoms	1.00																
Conduct Problems	.21	1.00															
Hyperactivity	.20	**.66**	1.00														
Peer Problems	.16	.10	.34	1.00													
Pro-Social Scale	-.03	**-.67**	**-.56**	-.16	1.00												
Total SDQ	**.53**	**.77**	**.85**	**.54**	**-.56**	1.00											
Inhibit	.12	**.81**	**.73**	**.29**	**-.59**	**.75**	1.00										
Shift	.24	**.64**	**.64**	**.42**	**-.45**	**.70**	**.65**	1.00									
Emotional	.38	**.77**	**.61**	.29	**-.47**	**.75**	**.78**	**.71**	1.00								
Initiate	.33	**.66**	**.69**	.29	**-.57**	**.73**	**.73**	**.64**	**.66**	1.00							
Working Memory	.28	**.64**	**.82**	**.58**	**-.49**	**.86**	**.81**	**.74**	**.75**	**.75**	1.00						
Plan/Organize	.38	**.63**	**.82**	**.42**	**-.65**	**.84**	**.64**	**.75**	**.68**	**.79**	**.78**	1.00					
Org Materials	-.12	.03	.33	.32	-.05	.21	.27	.14	.18	.39	.37	.33	1.00				
Monitor	**.44**	**.68**	**.58**	**.46**	**-.70**	**.79**	**.67**	**.60**	**.71**	**.80**	**.63**	**.78**	.13	1.00			
Behavioural Regulation	.28	**.83**	**.74**	.37	**-.56**	**.82**	**.91**	**.85**	**.93**	**.76**	**.86**	**.77**	.23	**.74**	1.00		
Metacognition	.24	**.72**	**.79**	**.46**	**-.73**	**.83**	**.75**	**.71**	**.69**	**.84**	**.81**	**.87**	**.44**	**.77**	**.80**	1.00	
Total BRIEF	.32	**.76**	**.82**	**.47**	**-.62**	**.88**	**.87**	**.81**	**.85**	**.88**	**.91**	**.90**	**.40**	**.82**	**.94**	**.91**	1.00

Significant correlations, $p < .05$, shown in bold script

Table 71 Mann Whitney U tests of SDQ scores in high and low sleep disturbance groups

	Low Sleep Disturbance (n=13)		High Sleep Disturbance (n= 12)		U test	
	Median	*IQR*	Median	*IQR*	*U*	*p**
Emotional Symptoms	2.00	2.00	2.00	3.00	74.00	.852
Conduct Problems	1.00	3.00	1.00	1.00	63.00	.437
Hyperactivity	3.00	3.00	4.00	4.00	75.50	.894
Peer Problems	1.00	4.00	0.50	2.00	6500	.503
Pro-social Scale	9.00	3.00	9.00	4.00	64.00	.470
Total SDQ	7.00	10.00	8.00	7.00	74.50	.852

* Exact significance

Table 72 Means and *SD* of BRIEF scores in high and low sleep disturbance groups

	Low sleep disturbance		High sleep disturbance	
	Mean	*SD*	Mean	*SD*
Inhibit	48.58	10.78	52.46	12.35
Shift	50.00	11.52	49.00	12.08
Emotional Control	52.17	12.12	53.23	10.70
Initiate	50.83	13.80	56.85	11.73
Working Memory	51.92	11.12	55.69	13.69
Plan/Organize	51.83	11.54	54.62	12.76
Organisation of Materials	52.50	10.73	57.77	9.04
Monitor	48.83	11.98	49.77	11.53
Behavioural Regulation	50.08	11.62	52.15	12.55
Metacognition	53.42	9.99	55.77	11.97
Total BRIEF	51.33	11.83	54.62	12.33

Table 73 Kolmogorov-Smirnov tests for actigraphy (CF and controls)

	D	df	*p*
Sleep Minutes	.080	77	.200*
Sleep Efficiency	.106	77	.031
Long Wake Episodes	.086	77	.200*
Wake after Sleep onset	.097	77	.071
Duration	.046	77	.200*
Sleep Latency	.085	77	.200*
Activity Index	.085	77	.200*

* This is a lower bound of the true significance.

Table 74 Kolmogorov-Smirnov tests for CSHQ (CF and controls)

	D	Df	*p*
Bedtime Resistance	.285	73	.000
Sleep Onset Delay	.294	73	.000
Sleep Duration	.275	73	.000
Sleep Anxiety	.414	73	.000
Night Wakings	.370	73	.000
Parasomnias	.193	73	.000
Sleep-Disordered Breathing	.360	73	.000
Daytime Sleepiness	.166	73	.000
Total CSHQ	.075	73	.200*

* This is a lower bound of the true significance.

Table 75 Kolmogorov-Smirnov tests for pulse oximetry (CF and controls)

	D	df	*p*
SpO_2 Nadir	.191	73	.000
SpO_2 mean	.207	73	.000
Desaturation index	.119	73	.013
No. of desaturations	.210	73	.000
Delta 12s Index	.240	73	.000
Time below95	.083	73	.200*

* This is a lower bound of the true significance.

Table 76 Kolmogorov-Smirnov tests for SDQ (CF and controls)

	D	df	*p*
Emotional Symptoms	.191	73	.000
Conduct Problems	.207	73	.000
Hyperactivity	.119	73	.013
Peer Problems	.210	73	.000
Pro-social scale	.240	73	.000
Total SDQ	.083	73	.200*

* This is a lower bound of the true significance.

Table 77 Kolmogorov-Smirnov tests for EF tests (CF and controls)

	D	df	*p*
Sky correct	.306	77	.000
Sky timing	.088	77	.200*
Sky attention	.127	77	.004
Score	.186	77	.000
Creature correct	.289	77	.000
Creature timing	.144	75	.001
Sky DT	.349	77	.000
Score DT	.152	77	.000
Same Worlds	.079	77	.200*
Opposite Worlds	.143	77	.001
Tower	.107	77	.029
Verbal Fluency	.104	77	.039
Digit recall	.196	77	.000
Backward Digit Recall	.155	77	.000
Spatial Span	.086	77	.200*
Coding	.095	77	.085
Symbol Search	.107	77	.028
Processing speed	.097	77	.069
Global executive function	.069	77	.200*

* This is a lower bound of the true significance.

Table 78 Kolmogorov-Smirnov tests for BRIEF (CF and controls)

	D	Df	*p*
Inhibition	.149	75	.000
Shifting	.149	75	.000
Emotional	.101	75	.056
Initiating	.128	75	.004
Working Memory	.073	75	.200*
Planning	.088	75	.200*
Organisation	.097	75	.078
Monitoring	.104	75	.045
Behavioural Regulation Index	.102	75	.052
Metacognition	.070	75	.200*
BRIEF total score	.122	75	.008

* This is a lower bound of the true significance.

Appendix D. Study 4 Additional Information

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Tel: 02380 594593
Email: slh604@soton.ac.uk

UNIVERSITY OF Southampton
School of Psychology
School of Medicine

Sleep, Learning, & Behaviour in Children with Cystic Fibrosis
Sleep Laboratory Study

Participant information sheet for parents

We would like to invite you and your child to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it would involve. Please read the following information carefully and discuss it with others if you wish. Take time to decide if you want your child to take part. If anything is unclear, or if you need to know more, please ask.

Who is running the study?
Mrs Simone Holley, PhD research student, School of Psychology, University of Southampton
Dr Catherine Hill, Senior Lecturer in Child Health, School of Medicine, University of Southampton
Drs Gary Connett and Julian Legg, Consultant Respiratory Paediatricians, Southampton University Hospitals NHS Trust
Professor Jim Stevenson, School of Psychology, University of Southampton

What is the purpose of the study?
Your child participated in the first phase of this project, which examined sleep disturbance using actigraphy and its relationship with attention and memory. The purpose of the second phase of the study is to obtain more detailed assessments of children's sleep using the sleep laboratory. We would like to know if the information that we obtained from the actigraphy can be supported by the sleep laboratory. This project forms part of a PhD thesis being conducted by Simone Holley, a PhD student in the School of Psychology.

Why has my child been chosen?
We have chosen 20 children to take part in this phase. 10 children were chosen because the actigraphy data showed that they had less sleep disturbance compared with the other children in the study. The other 10 children were chosen because the actigraphy data showed that they had greater sleep disturbance than the other children.

Do we have to take part?
You and your child's participation is voluntary, it is up to you to decide whether or not you wish to take part, but we would ask that you ensure your child understands what is involved and is willing to take part. If you agree to take part, you will be asked to sign a consent form but you should be aware that <u>even though you sign the consent form, you</u>

are still free to withdraw your child from the study at any time without giving reason. This would not affect the standard of care you receive.

What will happen to my child if they take part?

You will be asked to bring your child to the Children's Sleep laboratory in the Wellcome Trust Clinical Research Facility in Southampton General Hospital for an overnight sleep study. You would be asked to arrive about an hour before your child's usual bedtime. Your child will be asked to do a simple lung function test (spirometry) they will almost certainly have done this before. It involves blowing as hard as possible into a mouthpiece that then measures the amount of air blown out. Your child will be allowed some time to settle into the sleep laboratory before going to bed. Before your child goes to bed some sensors will be attached to different parts of his / her body these including the scalp, the chest, the chin and either side of the eyes. These all measure brain and muscle activity and tell us whether your child is asleep and what part of sleep they are in (i.e. dreaming or non-dreaming). The placement of the sensors is painless and most children are not bothered by this. We have a lot of experience with sleep studies and will try to work with as little fuss as possible. Your child will then be settled in bed for the night. You may stay in your child's room through the night and a separate bed is provided. Your child will be observed during sleep from a nearby monitoring stations and a digital video recording made of their movement in sleep. The camera field does not include the bed of the accompanying parent! The next morning you will be given breakfast before going home. A report from this sleep study, which can give useful diagnostic information, will go to your CF doctor.

What are the possible disadvantages and side-effects (risks) to my child if he / she takes part?

This study will not administer any treatments (medicines) and the procedures are unlikely to cause any harm or discomfort. In the unlikely event that you or your child finds any part of the study upsetting, you will have an opportunity to talk through your concerns with the researchers and withdraw your participation if you so wish.

What are the possible benefits of taking part?

We hope that you will find participating in this study an enjoyable experience. The information obtained from the sleep study will provide your child's CF doctor with information on your child's oxygen levels and breathing while asleep that may be useful to their care.

Will I be reimbursed for my travelling costs?

We will pay you any costs incurred in travelling to the hospital, such as petrol costs, train or bus fares or taxi costs. We will also pay for you parking whilst you are here.

What happens when the research study finishes?

The information obtained from your child and the other children will be put together and carefully analysed. (Please note that all information obtained from all children will be coded and remain anonymous.) Our findings will be reported in research articles and conferences in the UK and overseas. This will enable other doctors to learn from our study.

What if something goes wrong?

If you are concerned about any part of the study we advise you in the first instance to talk to the researchers (telephone numbers at the top). If you would like to take your

concerns further you may speak to your CF doctor and/or ask your doctor about the standard hospital complaints procedure.

Will the information obtained be confidential?

If you consent to take part in the study, your child's medical records will be accessed by the health professionals in the study. All information about your child that is collected during the course of the study will be kept strictly confidential. The results of your child's sleep study will only be sent to his / her CF doctor, and the psychology results will only be sent to you. Results of this study will not include your or your child's name, or any other identifying characteristics. Procedures for handling, processing, storage and destruction of data is compliant with the Data Protection Act 1998. Data will be stored anonymously and securely on disc for up to 15 years and then disposed of securely. Only authorised persons will have access to the data.

Who is organising and funding the research?

This study is being organised by those researchers whose names are listed at the top. A charitable Trust (Gerald Kerkut Charitable Trust) is providing the funding for the PhD research.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee (REC) to protect your safety, rights, wellbeing, and dignity. This study has been reviewed and given favourable opinion by the Southampton IOW, Portsmouth, and South East Hampshire Research and Ethics committee. This study has also been reviewed by the University of Southampton, School of Psychology Research Ethics Committee.

Complaints

If you have a concern about any aspect of this study or you wish to make a complaint, you may contact the Chair of the Ethics Committee, Department of Psychology, University of Southampton, Southampton, SO17 1BJ. Phone: (023) 8059 5578.

Contact for further information

If you have further questions please contact Simone Holley, at the University of Southampton on 02380594593, or email slh604@soton.ac.uk. Alternatively you may contact Dr Cathy Hill on xxxxxxxxxxxxx

Thank you for you time!

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UNIVERSITY OF Southampton
School of Psychology
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Sleep, Learning, & Behaviour in Children with Cystic Fibrosis
Sleep Laboratory Study

Information sheet for child

We are asking if you would like to take part in a research project to find out if your CF affects your sleep during the night. We are also trying to find out if children are better at learning when they sleep well. Before you decide to take part, it is important that you understand why the research is being done and what will happen to you. Please read this leaflet carefully and ask your mum or dad anything you do not understand.

What is research? Why is this project being done?
Research is way we try to find out the answers to questions. We want to find out if children with CF have trouble sleeping. We also want to know if sleep affects how well children can learn, pay attention, and remember things.

Why have I been asked to take part?
You took part in the first part of this study and we measured your sleep using the special watch called an actigraph. You have been chosen because the information from the watch suggests that you have either sleep very well or have trouble sleeping. We have invited 10 children to take part who may have a lot of sleep disturbance and 10 children who have very little sleep disturbance.

Did anyone else check the study is OK to do?
Before any research is allowed to happen, it has to be checked by a group of people called a Research Ethics Committee. They make sure the research is fair. This project has been checked by the Southampton Isle of Wight, Portsmouth, and South East Hampshire Research Ethics Committee.

Do I have to take part?
No! It is up to YOU. You must only take part if you want to, and if your parents are happy for you to take part. If you do agree to take part you will be asked to sign a form (write your name) saying that you are happy to take part. <u>You are free to stop taking part at any time during the research without giving a reason.</u> If you decide to stop taking part it will not affect the care you receive.

What will happen to me if I take part?
Your mum or dad will bring you to a special children's sleep centre at Southampton General Hospital. You and your parent will sleep there for one night. You will arrive

in the evening before you go to bed. When you arrive we will measure how well you can blow air out of your mouth by using a spirometer, you will have probably done this with a doctor or nurse before. Before you go to bed we will put sensors on different parts of your body including your head, chest, chin and either side of your eyes. These tell us whether you are asleep. We will also measure your breathing using stretchy bands around your chest and tummy as well as soft tubes taped between your nose and mouth. The placement of the sensors does not hurt and most children are not bothered by this. You will then be allowed to go to sleep and your mum or dad can stay in your room through the night. We will be monitoring you throughout your sleep from a nearby room and will also be making a video recording of your sleep.

Is there anything for me to be worried about?
We have done lots of sleep studies before with children. The sleep study should not hurt or be uncomfortable. If you find anything uncomfortable, or it upsets you can ask to stop.

Will my medical details be kept private if I take part? Will anyone else know I'm doing this?
Only the researchers involved in the project and your doctors will know you are taking part.

Will I have fun?
You may think it exciting to come to the special sleep centre and see all the special equipment that we use to measure your sleep.

If you have any questions or there is anything you don't understand you can ask the researcher who comes to your home or your parents.

UNIVERSITY OF Southampton
School of Psychology
School of Medicine

Sleep, Learning, and Behaviour in children with Cystic Fibrosis
Sleep laboratory study

Parent Consent Form

Please initial boxes

8. I confirm that I have read and understood the information sheet dated ……. for the above study (version……). I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily. ☐

9. I understand that my child's participation is voluntary and that I am free to withdraw my child at any time, without giving any reason, without my child's medical care or legal rights being affected. ☐

10. I give permission for the researchers involved in the project to have access to my child's medical records. ☐

11. I agree to allow the named researchers to store anonymized results and digital film images obtained from my child on a CD disc/Hospital or University computer for up to 15 years after the study. ☐

12. I understand that I will need to complete questionnaires about my child for the study ☐

13. I agree to let my child take part in the above study. ☐

_____ _____ _____
Name of parent Date Parent's Signature

_____ _____ _____
Researcher Date Signature

The study has been described to my child. I am satisfied that he/she is happy to take part. I understand that I may withdraw them from the study at any time if I believe they are unhappy.

_____ _____ _____
Name of parent Date Parent's Signature
(1 copy for parent, research file and hospital notes)

UNIVERSITY OF Southampton
School of Psychology
School of Medicine

Sleep, Learning, & Behaviour in Children with Cystic Fibrosis
Sleep Laboratory study

Consent form for child

Have you read (or had read to you) about this project?	Yes/No
Has somebody else explained this project to you?	Yes/No
Do you understand what this project is about?	Yes/No
Have you asked all the questions you want?	Yes/No
If you asked any questions- Have they been answered in a way you understand?	Yes/No
Do you understand it's OK to stop taking part at any time?	Yes/No
Are you happy to take part?	Yes/No

If you <u>don't</u> want to take part, <u>don't</u> write your name!

If you <u>do</u> want to take part, please write your name and today's date

Your name _____

Date _____

Name of Researcher: _____

Signature: _____

Appendix E. Child Sleep Habits Questionnaire

Child's Sleep Habits
(Preschool and School-Aged)

_____
Coding

The following statements are about your child's sleep habits and possible difficulties with sleep. Think about the past week in your child's life when answering the questions. If last week was unusual for a specific reason (such as your child had an ear infection and did not sleep well or the TV set was broken), choose the most recent typical week. Answer USUALLY if something occurs **5 or more times** in a week; answer SOMETIMES if it occurs **2-4 times** in a week; answer RARELY if something occurs **never or 1 time** during a week. Also, please indicate whether or not the sleep habit is a problem by circling "Yes," "No," or "Not applicable (N/A).

Bedtime

Write in child's bedtime: _____

	3 Usually (5-7)	2 Sometimes (2-4)	1 Rarely (0-1)	Problem?		
Child goes to bed at the same time at night	☐	☐	☐	Yes	No	N/A
Child goes to bed at the same time at night	☐	☐	☐	Yes	No	N/A
Child falls asleep within 20 minutes after going to bed	☐	☐	☐	Yes	No	N/A
Child falls asleep alone in own bed	☐	☐	☐	Yes	No	N/A
Child falls asleep in parent's or sibling's bed	☐	☐	☐	Yes	No	N/A
Child falls asleep with rocking or rhythmic movements	☐	☐	☐	Yes	No	N/A
Child needs special object to fall asleep (doll, special blanket, etc.)	☐	☐	☐	Yes	No	N/A
Child needs parent in the room to fall asleep	☐	☐	☐	Yes	No	N/A
Child is ready to go to bed at bedtime	☐	☐	☐	Yes	No	N/A
Child resists going to bed at bedtime	☐	☐	☐	Yes	No	N/A
Child struggles at bedtime (cries, refuses to stay in bed, etc.)	☐	☐	☐	Yes	No	N/A
Child is afraid of sleeping in the dark	☐	☐	☐	Yes	No	N/A
Child is afraid of sleep alone	☐	☐	☐	Yes	No	N/A

Sleep Behavior

Child's usual amount of sleep each day: _____ hours and _____ minutes
(combining nighttime sleep and naps)

	3 Usually (5-7)	2 Sometimes (2-4)	1 Rarely (0-1)	Problem?		
Child sleeps too little	☐	☐	☐	Yes	No	N/A
Child sleeps too much	☐	☐	☐	Yes	No	N/A
Child sleeps the right amount	☐	☐	☐	Yes	No	N/A
Child sleeps about the same amount each day	☐	☐	☐	Yes	No	N/A
Child wets the bed at night	☐	☐	☐	Yes	No	N/A
Child talks during sleep	☐	☐	☐	Yes	No	N/A
Child is restless and moves a lot during sleep	☐	☐	☐	Yes	No	N/A
Child sleepwalks during the night	☐	☐	☐	Yes	No	N/A
Child moves to someone else's bed during the night (parent, brother, sister, etc.)	☐	☐	☐	Yes	No	N/A

 CSHQ

Coding

Sleep Behavior (continued)

	3 Usually (5-7)	2 Sometimes (2-4)	1 Rarely (0-1)	Problem?		
Child reports body pains during sleep. If so, where? _____	☐	☐	☐	Yes	No	N/A
Child grinds teeth during sleep (your dentist may have told you this)	☐	☐	☐	Yes	No	N/A
Child snores loudly	☐	☐	☐	Yes	No	N/A
Child seems to stop breathing during sleep	☐	☐	☐	Yes	No	N/A
Child snorts and/or gasps during sleep	☐	☐	☐	Yes	No	N/A
Child has trouble sleeping away from home (visiting relatives, vacation)	☐	☐	☐	Yes	No	N/A
Child complains about problems sleeping	☐	☐	☐	Yes	No	N/A
Child awakens during night screaming, sweating, and inconsolable	☐	☐	☐	Yes	No	N/A
Child awakens alarmed by a frightening dream	☐	☐	☐	Yes	No	N/A

Waking During the Night

	3 Usually (5-7)	2 Sometimes (2-4)	1 Rarely (0-1)	Problem?		
Child awakes once during the night	☐	☐	☐	Yes	No	N/A
Child awakes more than once during the night	☐	☐	☐	Yes	No	N/A
Child returns to sleep without help after waking	☐	☐	☐	Yes	No	N/A

Write the number of minutes a night waking usually lasts: _____

Morning Waking

Write in the time of day child usually wakes in the morning: _____

	3 Usually (5-7)	2 Sometimes (2-4)	1 Rarely (0-1)	Problem?		
Child wakes up by him/herself	☐	☐	☐	Yes	No	N/A
Child wakes up with alarm clock	☐	☐	☐	Yes	No	N/A
Child wakes up in negative mood	☐	☐	☐	Yes	No	N/A
Adults or siblings wake up child	☐	☐	☐	Yes	No	N/A
Child has difficulty getting out of bed in the morning	☐	☐	☐	Yes	No	N/A
Child takes a long time to become alert in the morning	☐	☐	☐	Yes	No	N/A
Child wakes up very early in the morning	☐	☐	☐	Yes	No	N/A
Child has a good appetite in the morning	☐	☐	☐	Yes	No	N/A

Coding

Daytime Sleepiness

	3 Usually (5-7)	2 Sometimes (2-4)	1 Rarely (0-1)	Problem?		
Child naps during the day	☐	☐	☐	Yes	No	N/A
Child suddenly falls asleep in the middle of active behavior	☐	☐	☐	Yes	No	N/A
Child seems tired	☐	☐	☐	Yes	No	N/A

During the past week, your child has appeared very sleepy or fallen asleep during the following (check all that apply):

	1 Not Sleepy	2 Very Sleepy	3 Falls Asleep
Play alone	☐	☐	☐
Watching TV	☐	☐	☐
Riding in car	☐	☐	☐
Eating meals	☐	☐	☐

Appendix F. Oximetry

Sleep, Learning, & Behaviour in Children
Oximeter Instructions

The oximeter will measure how much oxygen your child is getting throughout the night via a finger probe that looks like a large plaster. If your child is allergic to elastoplast please do not use the oximeter. If possible please use the oximeter for two or three consecutive nights, however, if your child finds the oximeter uncomfortable, discontinue after one night.

1. Plug the oximeter into a mains socket. If the unit is plugged in correctly, the two lights on the left hand side should be illuminated. If not check the power cable is plugged in properly, and that the removable unit is pushed in properly. If the unit loses power throughout the night it will start to beep!

2. Attach the plaster probe to the child's index or middle finger of the non-dominant hand (see overleaf). This probe will need to be reused so it is helpful to save the adhesive backing. Please tape the wire at the wrist, you may find it easier to wrap the actiwatch around the probe wire, this will help to hold the probe in place.

3. The metallic end of the probe plugs into a small slot on the accompanying lead, which is in turn plugged into the slot on the right hand side (marked A on diagram) of the oximeter (you need to press the two grey buttons on the plug to remove it).

4. Once the probe is on place and connected to the oximeter, turn the oximeter on by pressing the on/off button, this will automatically start recording your child's oxygen levels. You will know it is working because the display will show a number on the left hand side, which is the oxygen saturation, (usually between 95 and 100) and a number on the right hand side (your child's pulse). A red light will glow from the finger probe.

5. As this oximeter is usually used in hospital settings, the unit is automatically programmed to sound an alarm if the probe falls off, or if the oxygen level drops very low. This means that every time the oximeter is switched on, you must turn the alarm settings off. To do this, press button 2, you will see a Menu, Alarms is at the top, press button 2 which will select the alarm menu. Press button 4 (south

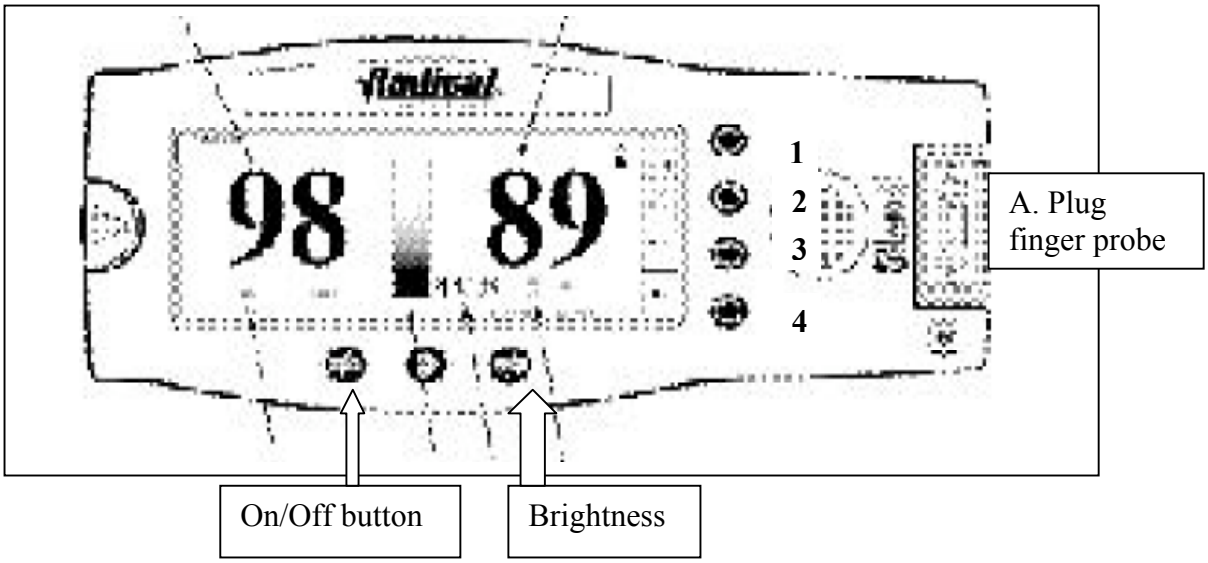
facing arrow) 4 times, which will highlight the silence setting which will be set to 120 sec. Press button 2, then press button 3 (north facing arrow) once which will select All Mute. Press button 2, you will be asked to confirm, press button 4 (a tick). Then press button 1 two times to return to the normal display.

6. If the display is too bright, pressing the brightness button should dull the display.

7. If your child needs to go to the toilet, you can detach the probe wire, and then reattach as soon as possible.

8. In the morning when your child wakes, just press the same button you used to turn it on and carefully remove the plaster probe from the finger and reattach the adhesive backing, so that it can be reused the following night.

9. When reattaching the probe on consecutive nights wrap some sticky tape around the probe to ensure good adhesion.



Instructions for attaching plaster finger probe

1. Remove from packet and familiarise yourself with the probe.
2. Remove adhesive baking from finger probe, lay probe flat in front of child's hand, with white side showing, and metallic end furthest away from child's hand.
3. Place index or middle finger on black square and stick the two rounded ends around the finger (see Fig. 2a)
4. Take hold of the metallic end, and fold down over the length of the finger, and fold the two sides down (Fig. 2b). If the finger probe is in place, the position of the child's finger should match the position of the diagram on the probe (see Fig. 2c).

Any problems please don't hesitate to call me!

Appendix G. Actigraphy Information

An actigraph is a small, lightweight, limb-worn electronic device about the size of a watch. It is typically worn on the wrist (or ankle) and measures long-term gross motor activity and enables temporal and qualitative aspects of sleep to be recorded. The actigraph contains an accelerometer that is capable of sensing any motion with minimal resultant force of 0.01g. The actigraph can record data continuously for up to 22 days, which can then be downloaded to a computer and specialist software is used to analyze the data giving temporal and qualitative measures of sleep. Validation studies have demonstrated a 90% agreement rate between actigraphy and PSG for normal subjects (Sadeh et al., 1989). An algorithm has been developed to analyze the data that has been validated using children (Sadeh, Sharkey, & Carskadon, 1994). The actigraph software generates numerous sleep variables, not all of which are referred to in this data analysis.

Appendix H. Strengths & Difficulties Questionnaire

Strengths and Difficulties Questionnaire

For each item, please mark the box for Not True, Somewhat True or Certainly True. It would help us if you answered all items as best you can even if you are not absolutely certain or the item seems daft! Please give your answers on the basis of the child's behaviour over the last six months or this school year.

Child's Name ..... Male/Female

Date of Birth.....

	Not True	Somewhat True	Certanly True
Considerate of other people's feelings	☐	☐	☐
Restless, overactive, cannot stay still for long	☐	☐	☐
Often complains of headaches, stomach-aches or sickness	☐	☐	☐
Shares readily with other children (treats, toys, pencils etc.)	☐	☐	☐
Often has temper tantrums or hot tempers	☐	☐	☐
Rather solitary, tends to play alone	☐	☐	☐
Generally obedient, usually does what adults request	☐	☐	☐
Many worries, often seems worried	☐	☐	☐
Helpful if someone is hurt, upset or feeling ill	☐	☐	☐
Constantly fidgeting or squirming	☐	☐	☐
Has at least one good friend	☐	☐	☐
Often fights with other children or bullies them	☐	☐	☐
Often unhappy, down-hearted or tearful	☐	☐	☐
Generally liked by other children	☐	☐	☐
Easily distracted, concentration wanders	☐	☐	☐
Nervous or clingy in new situations, easily loses confidence	☐	☐	☐
Kind to younger children	☐	☐	☐
Often lies or cheats	☐	☐	☐
Picked on or bullied by other children	☐	☐	☐
Often volunteers to help others (parents, teachers, other children)	☐	☐	☐
Thinks things out before acting	☐	☐	☐
Steals from home, school or elsewhere	☐	☐	☐
Gets on better with adults than with other children	☐	☐	☐
Many fears, easily scared	☐	☐	☐
Sees tasks through to the end, good attention span	☐	☐	☐

Signature ..... Date .....

Parent/Teacher/Other (please specify:)

Name: _____

Sleep Diary

Please try and ensure this diary is completed accurately and every day

Day	I woke up at	I went to bed at	I fell asleep at	I took the actiwatch off
e.g. Sunday	*7am*	*8.30pm*	*9pm*	*12-1pm 7-7.30pm*

REFERENCES

Akerstedt, T., Fredlund, P., Gillberg, M., & Jansson, B. (2002). A prospective study of fatal occupational accidents - relationship to sleeping difficulties and occupational factors. *Journal of Sleep Research, 11*, 69-71.

Alexander, M. P., & Stuss, D. T. (2000). Disorders of frontal lobe functioning. *Seminars in Neurology, 20*(4), 427-437.

Ali, N. J., Pitson, D., & Stradling, J. R. (1996). Sleep disordered breathing: effects of adenotonsillectomy on behaviour and psychological functioning. *European Journal of Pediatrics, 155*(1), 56-62.

Ali, N. J., Pitson, D. J., & Stradling, J. R. (1993). Snoring, sleep disturbance, and behavior in 4-5 Year Olds. *Archives of Disease in Childhood, 68*(3), 360-366.

Alloway, T., Gathercole, S. E., Kirkwood, H., & Elliott, J. (2008). Evaluating the validity of the Automated Working Memory Assessment. *Educational Psychology: An International Journal of Experimental Educational Psychology, 28*(7), 725 - 734.

Alloway, T. P., Gathercole, S. E., & Pickering, S. J. (2004). Automated Working Memory Assessment. Computerised test battery.

American Sleep Disorders Association. Diagnostic Classification Steering Committee. (1990). *The International classification of sleep disorders: diagnostic and coding manual*. Rochester, MN: American Sleep Disorders Association.

Amin, R., Bean, J., Burklow, K., & Jeffries, J. (2005). The relationship between sleep disturbance and pulmonary function in stable pediatric cystic fibrosis patients. *Chest, 128*(3), 1357-1363.

Anderson, P. (2002). Assessment and development of executive function (EF) during childhood. *Child Neuropsychology, 8*(2), 71-82.

Anderson, S. W., Damasio, H., Jones, R. D., & Tranel, D. (1990, Feb). *Wisconsin card sorting test-performance as a measure of frontal-lobe damage.* Paper presented at the 18th Annual Meeting of the International Neuropsychological Soc, Orlando, Fl.

Anderson, V. (2001). Assessing executive functions in children: biological, psychological, and developmental considerations. *Developmental Neurorehabilitation, 4*(3), 119 - 136.

Annett, R. D., Aylward, E. H., Lapidus, J., Bender, B. G., DuHamel, T., & Childhood Asthma Management, P. (2000). Neurocognitive functioning in children with

mild and moderate asthma in the Childhood Asthma Management Program. *Journal of Allergy and Clinical Immunology, 105*(4), 717-724.

Aronen, E. T., Paavonen, E. J., Fjallberg, M., Soininen, M., & Torronen, J. (2000). Sleep and psychiatric symptoms in school-age children. *Journal of the American Academy of Child and Adolescent Psychiatry, 39*(4), 502-508.

Aserinsky, E., & Kleitman, N. (1953). Regularly occurring periods of eye motility, and concomitant phenomena, during sleep *Science, 118*(3062), 273-274.

Aserinsky, E., & Kleitman, N. (1955). Two types of ocular motility occurring in sleep. *Journal of Applied Physiology, 8*(1), 1-10.

Atkinson, R. C., & Shiffrin, R. M. (1968). Human memory: A proposed system and its control processes. In K. W. Spence & J. T. Spence (Eds.), *The psychology of learning and motivation* (Vol. 8). London: Academic Press.

Baddeley, A. D. (1986). *Working memory*. Oxford: Clarendon.

Baddeley, A. D. (1996). Exploring the central executive. *Quarterly Journal of experimental psychology, 49a*, 5-28.

Baddeley, A. D. (1997). *Human memory: theory and practice* (Rev. ed.). Hove: Psychology.

Baddeley, A. D. (2000). The episodic buffer: a new component of working memory? *Trends in Cognitive Science, 4*(11), 417-423.

Baddeley, A. D. (2001). Is working memory still working? *American Psychologist, 56*(11), 851-864.

Baddeley, A. D., & Hitch, G. J. (1974). Working memory. In G. A. Bower (Ed.), *Recent advances in learning and motivation* (Vol. 8, pp. 47-90). New York: Academic Press.

Baillargeon, R., Graber, M., Devos, J., & Black, J. (1990). Why do young infants fail to search for hidden objects. *Cognition, 36*(3), 255-284.

Barkley, R. A. (1997). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. *Psychological Bulletin, 121*(1), 65-94.

Bass, J. L., Corwin, M., Gozal, D., Moore, C., Nishida, H., Parker, S., et al. (2004). The effect of chronic or intermittent hypoxia on cognition in childhood: A review of the evidence. *Pediatrics, 114*(3), 805-816.

Beebe, D. W., & Gozal, D. (2002). Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to

daytime cognitive and behavioral deficits. *Journal of Sleep Research, 11*(1), 1-16.

Beebe, D. W., Groesz, L., Wells, C., Nichols, A., & McGee, K. (2003). The neuropsychological effects of obstructive sleep apnea: A meta-analysis of norm-referenced and case-controlled data *Sleep, 26*(3), 298-307.

Bell, M. A., & Fox, N. A. (1992). The relations between frontal brain electrical-activity and cognitive-development during infancy. *Child Development, 63*(5), 1142-1163.

Benes, F. M. (2001). The development of prefrontal cortex: The maturation of neurotransmitter systems and their interactions. In C. A. Nelson & M. Luciana (Eds.), *Handbook of developmental cognitive neuroscience*. Cambridge, MA: MIT Press.

Bland, J. M., & Altman, D. G. (1997). Cronbach's alpha. *BMJ, 314*(7080), 572.

Bliwise, D. L. (1993). Sleep in normal aging and dementia *Sleep, 16*(1), 40-81.

Blunden, S., Lushington, K., & Kennedy, D. (2001). Cognitive and behavioural performance in children with sleep-related obstructive breathing disorders. *Sleep Medicine Reviews, 5*(6), 447-461.

Blunden, S., Lushington, K., Kennedy, D., Martin, J., & Dawson, D. (2000). Behavior and neurocognitive performance in children aged 5-10 years who snore compared to controls. *Journal of Clinical and Experimental Neuropsychology, 22*(5), 554-568.

Bohadana, A. B., Hannhart, B., & Teculescu, D. B. (2002). Nocturnal worsening of asthma and sleep-disordered breathing. *Journal of Asthma, 39*(2), 85-100.

Bonnet, M. H., & Arand, D. L. (2003). Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Medicine Reviews, 7*(4), 297-310.

Born, J., Rasch, B., & Gais, S. (2006). Sleep to Remember. *Neuroscientist, 12*(5), 410-424.

Bradley, S., Solin, P., Wilson, J., Johns, D., Walters, E. H., & Naughton, M. T. (1999). Hypoxemia and hypercapnia during exercise and sleep in patients with cystic fibrosis. *Chest, 116*(3), 647-654.

Braun, A. R., Balkin, T. J., Wesensten, N. J., Carson, R. E., Varga, M., Baldwin, P., et al. (1997). Regional cerebral blood flow throughout the sleep-wake cycle - an (H2O)-O-15 PET study. *Brain, 120*, 1173-1197.

Bull, R., Espy, K. A., & Senn, T. E. (2004). A comparison of performance on the Towers of London and Hanoi in young children. *Journal of Child Psychology and Psychiatry, 45*(4), 743-754.

Burgess, P. W. (1997). Theory and methodolody in executive function research. In P. M. A. Rabbitt (Ed.), *Methodology of Frontal and Executive Function*. Hove: UK: Psychology Press.

Calam, R., Gregg, L., & Goodman, R. (2005). Psychological adjustment and asthma in children and adolescents: The UK nationwide mental health survey. *Psychosomatic Medicine, 67*(1), 105-110.

Carskadon, M. A., Acebo, C., & Jenni, O. G. (2004). Regulation of adolescent sleep - Implications for behavior. *Adolescent Brain Development: Vulnerabilities and Opportunities, 1021*, 276-291.

Casey, B. J., Giedd, J. N., & Thomas, K. M. (2000). Structural and functional brain development and its relation to cognitive development. *Biological Psychology, 54*(1-3), 241-257.

Cato, M. A., Delis, D. C., Abildskov, T. J., & Bigler, E. (2004). Assessing the elusive cognitive deficits associated with ventromedial prefrontal damage: A case of a modern-day Phineas Gage. *Journal of the International Neuropsychological Society, 10*(3), 453-465.

Chelune, G. J., & Baer, R. A. (1986). Developmental norms for the Wisconsin Card Sorting test. *Journal of Clinical and Experimental Neuropsychology, 8*(3), 219-228.

Chervin, R. D., Archbold, K. H., Dillon, J. E., Panahi, P., Pituch, K. J., Dahl, R. E., et al. (2002). Inattention, hyperactivity, and symptoms of sleep-disordered breathing. *Pediatrics, 109*(3), 449-456.

Chervin, R. D., Dillon, J. E., Archbold, K. H., & Ruzicka, D. L. (2003). Conduct problems and symptoms of sleep disorders in children. *Journal of the American Academy of Child and Adolescent Psychiatry, 42*(2), 201-208.

Chervin, R. D., Dillon, J. E., Bassetti, C., Ganoczy, D. A., & Pituch, K. J. (1997). Symptoms of sleep disorders, inattention, and hyperactivity in children. *Sleep, 20*(12), 1185-1192.

Chervin, R. D., Hedger, K., Dillon, J. E., & Pituch, K. J. (2000). Pediatric sleep questionnaire (PSQ): validity and reliability of scales for sleep-disordered breathing, snoring, sleepiness, and behavioral problems. *Sleep Medicine, 1*(1), 21-32.

Chervin, R. D., Murman, D. L., Malow, B. A., & Totten, V. (1999). Cost-utility of three approaches to the diagnosis of sleep apnea: Polysomnography, home testing, and empirical therapy. *Annals of Internal Medicine, 130*(6), 496-+.

Chervin, R. D., Ruzicka, D. L., Giordani, B. J., Weatherly, R. A., Dillon, J. E., Hodges, E. K., et al. (2006). Sleep-disordered breathing, behavior, and cognition in children before and after adenotonsillectomy. *Pediatrics, 117*(4), E769-E778.

Coble, P. A., Kupfer, D. J., Taska, L. S., & Kane, J. (1984). EEG sleep of normal healthy children. Findings using standard measurement methods. *Sleep, 7*(4), 289-303.

Cohen, J. D., Aston-Jones, G., & Gilsenrat, M. S. (2004). A systems-level perspective on attention and cognitive control: Guided activation, adaptive gating, conflict monitoring, and exploitation versus exploration. In M. I. Posner (Ed.), *Cognitive Neuroscience of Attention* (pp. 71-90). New York ; London: Guilford Press.

Cohen-Zion, M., & Ancoli-Israel, S. (2004). Sleep in children with attention-deficit hyperactivity disorder (ADHD): a review of naturalistic and stimulant intervention studies. *Sleep Medicine Reviews, 8*(5), 379-402.

Corkum, P., Tannock, R., & Moldofsky, H. (1998). Sleep disturbances in children with attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 37*(6), 637-646.

Corkum, P., Tannock, R., Moldofsky, H., Hogg-Johnson, S., & Humphries, T. (2001). Actigraphy and parental ratings of sleep in children with attention-deficit-hyperactivity disorder (ADHD) *Sleep, 24*(3), 303-312.

Cortina, J. M. (1993). What is coefficient alpha? An examination of theoy and applications. *Journal of Applied Psychology, 78*, 98-104.

Curzi-Dascalova, L., Peirano, P., & Morel-Kahn, F. (1988). Development of sleep states in normal premature and full-term newborns. *Developmental Psychobiology, 21*(5), 431-444.

Dancey, D. R., Tullis, E. D., Heslegrave, R., Thornley, K., & Hanly, P. J. (2002). Sleep quality and daytime function in adults with cystic fibrosis and severe lung disease. *European Respiratory Journal, 19*(3), 504-510.

Desager, K. N., Nelen, V., Weyler, J. J. J., & De Backer, W. A. (2005). Sleep disturbance and daytime symptoms in wheezing school-aged children. *Journal of Sleep Research, 14*(1), 77-82.

Diamond, A. (1988). Abilities and neural mechanisms underlying ab performance. *Child Development, 59*(2), 523-527.

Diamond, A., & Doar, B. (1989). The performance of human infants on a measure of frontal-cortex function, the delayed-response task. *Developmental Psychobiology, 22*(3), 271-294.

Diamond, A., & Taylor, C. (1996). Development of an aspect of executive control: Development of the abilities to remember what I said and to "Do as I say, not as I do". *Developmental Psychobiology, 29*(4), 315-334.

Dobbin, C. J., Bartlett, D., Melehan, K., Grunstein, R. R., & Bye, P. T. P. (2005). The Effect of Infective Exacerbations on Sleep and Neurobehavioral Function in Cystic Fibrosis. *American Journal of Respiratory and Critical Care Medicine, 172*(1), 99-104.

Dollman, J., Ridley, K., Olds, T., & Lowe, E. (2007). Trends in the duration of school-day sleep among 10- to 15-year-old South Australians between 1985 and 2004. *Acta PÊdiatrica, 96*(7), 1011-1014.

Drummond, S. P. A., & Brown, G. G. (2001). The effects of total sleep deprivation on cerebral responses to cognitive performance. *Neuropsychopharmacology, 25*, S68-S73.

Drummond, S. P. A., Brown, G. G., Gillin, J. C., Stricker, J. L., Wong, E. C., & Buxton, R. B. (2000). Altered brain response to verbal learning following sleep deprivation 68. *Nature, 403*(6770), 655-657.

Drummond, S. P. A., Brown, G. G., Stricker, J. L., Buxton, R. B., Wong, E. C., & Gillin, J. C. (1999). Sleep deprivation-induced reduction in cortical functional response to serial subtraction. *Neuroreport, 10*(18), 3745-3748.

Drummond, S. P. A., Gillin, J. C., & Brown, G. G. (2001). Increased cerebral response during a divided attention task following sleep deprivation 66. *Journal of Sleep Research, 10*(2), 85-92.

Duncan, J., Emslie, H., Williams, P., Johnson, R., & Freer, C. (1996). Intelligence and the frontal lobe: The organization of goal-directed behavior. *Cognitive Psychology, 30*(3), 257-303.

Durmer, J. S., & Dinges, D. F. (2005). Neurocognitive consequences of sleep deprivation. *Seminars in Neurology, 25*(1), 117-129.

El-Ad, B., & Lavie, P. (2005). Effect of sleep apnea on cognition and mood. *International Review of Psychiatry, 17*(4), 277 - 282.

El-Sheikh, M., Buckhalt, J. A., Mize, J., & Acebo, C. (2006). Marital conflict and disruption of children's sleep. *Child Development, 77*(1), 31-43.

Engle, R. W., Tuholski, S. W., Laughlin, J. E., & Conway, A. R. (1999). Working memory, short-term memory, and general fluid intelligence: a latent-variable approach. *Journal of Experimental Psychology: General, 128*(3), 309-331.

Engleman, H. M., & Douglas, N. J. (2004). Sleep 4: Sleepiness, cognitive function, and quality of life in obstructive sleep apnoea/hypopnoea syndrome. *Thorax, 59*(7), 618-622.

Eslinger, P. J., & Damasio, A. R. (1985). Severe disturbance of higher cognition after bilateral frontal-lobe ablation - patient EVR. *Neurology, 35*(12), 1731-1741.

Espy, K. A., Kaufmann, P. M., Glisky, M. L., & McDiarmid, M. D. (2001). New procedures to assess executive functions in preschool children. *Clinical Neuropsychologist, 15*(1), 46-58.

Espy, K. A., Kaufmann, P. M., McDiarmid, M. D., & Glisky, M. L. (1999). Executive functioning in preschool children: Performance on A-not-B and other delayed response format tasks. *Brain and Cognition, 41*(2), 178-199.

Everson, C. A., Bergmann, B. M., & Rechtschaffen, A. (1989). Sleep-deprivation in the rat III. Total sleep-deprivation. *Sleep, 12*(1), 13-21.

Fallone, G., Acebo, C., Seifer, R., & Carskadon, M. A. (2005). Experimental restriction of sleep opportunity in children: effects on teacher ratings. *Sleep, 28*(12), 1561-1567.

Ferber, R., & Guilleminault, C. (1987). The Sleepless Child. In *Sleep and its disorders in children* (pp. 141-163). New York: Raven Press.

Finelli, L. A., Borbely, A. A., & Achermann, P. (2001). Functional topography of the human non-REM sleep electroencephalogram. *European Journal of Neuroscience, 13*(12), 2282-2290.

Fry, A. F., & Hale, S. (1996). Processing speed, working memory, and fluid intellignece: Evidence for a developmental cascade. *Psychological Science, 7*, 237-241.

Fry, A. F., & Hale, S. (2000). Relationships among processing speed, working memory, and fluid intelligence in children. *Biological Psychology, 54*(1-3), 1-34.

Fuster, J. n. M. (1997). *The prefrontal cortex: anatomy, physiology, and neuropsychology of the frontal lobe* (3rd ed.). Philadelphia: Lippincott-Raven.

Gais, S., & Born, J. (2004). Declarative memory consolidation: Mechanisms acting during human sleep. *Learning & Memory, 11*(6), 679-685.

Gaudreau, H., Carrier, J., & Montplaisir, J. (2001). Age-related modifications of NREM sleep EEG: from childhood to middle age. *Journal of Sleep Research, 10*(3), 165-172.

George, C. F. (2004). Sleep 5: Driving and automobile crashes in patients with obstructive sleep apnoea/hypopnoea syndrome. *Thorax, 59*(9), 804-807.

Giedd, J. N., Blumenthal, J., Jeffries, N. O., Castellanos, F. X., Liu, H., Zijdenbos, A., et al. (1999). Brain development during childhood and adolescence: a longitudinal MRI study. *Nature Neuroscience, 2*(10), 861-863.

Gioia, G. A., Isquith, P. K., Guy, S. C., & Kenworthy, L. (2000). Behavior rating inventory of executive function. *Child Neuropsychology, 6*(3), 235-238.

Godefroy, O., Cabaret, M., Petit-Chenal, V., Pruvo, J. P., & Rousseaux, M. (1999). Control functions of the frontal lobes. Modularity of the central-supervisory system? *Cortex, 35*(1), 1-20.

Goldberg, E. (2001). *The executive brain: frontal lobes and the civilized mind*. Oxford ; New York: Oxford University Press.

Goodman, R. (1997). The Strengths and Difficulties Questionnaire: a research note. *Journal of Child Psychology and Psychiatry, 38*(5), 581-586.

Goodman, R. (2001). Psychometric Properties of the Strengths and Difficulties Questionnaire. *Journal of Amer Academy of Child & Adolescent Psychiatry, 40*(11), 1337-1345.

Goodman, R., & Scott, S. (1999). Comparing the Strengths and Difficulties Questionnaire and the Child Behavior Checklist: is small beautiful? *Journal of Abnormal Child Psychology, 27*(1), 17-24.

Gottlieb, D. J., Chase, C., Vezina, R. M., Heeren, T. C., Corwin, M. J., Auerbach, S. H., et al. (2004). Sleep-disordered breathing symptoms are associated with poorer cognitive function in 5-year-old children. *Journal of Pediatrics, 145*(4), 458-464.

Gozal, D. (1998). Sleep-disordered breathing and school performance in children. *Pediatrics, 102*(3), 616-620.

Gozal, D., & Pope, D. W. (2001). Snoring During Early Childhood and Academic Performance at Ages Thirteen to Fourteen Years. *Pediatrics, 107*(6), 1394-1399.

Hale, S. (1990). A global developmental trend in cognitive processing speed. *Child Development, 61*(3), 653-663.

Harrison, Y., & Horne, J. A. (1998). Sleep loss impairs short and novel language tasks having a prefrontal focus. *Journal of Sleep Research, 7*(2), 95-100.

Harrison, Y., & Horne, J. A. (2000). The impact of sleep deprivation on decision making: A review 1. *Journal of Experimental Psychology-Applied, 6*(3), 236-249.

Hayes, D., Jr. (2006). Obstructive sleep apnea syndrome: a potential cause of lower airway obstruction in cystic fibrosis. *Sleep Med, 7*(1), 73-75.

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.

Hill, C. M., Hogan, A. M., Onugha, N., Harrison, D., Cooper, S., McGrigor, V. J., et al. (2006). Increased cerebral blood flow velocity incChildren with mild sleep-disordered breathing: A possible association with abnormal neuropsychological function. *Pediatrics, 118*(4), e1100-1108.

Hiscock, H., & Wake, M. (2001). Infant sleep problems and postnatal depression: A community-based study. *Pediatrics, 107*(6), 1317-1322.

Holley, S., Hill, C. M., & Stevenson, J. (accepted for publication). A comparison of actigraphy and parental report of sleep habits in typically developing children aged 6-11 years. *Behavioural Sleep Medicine*.

Honomichl, R. D., Goodlin-Jones, B. L., Burnham, M., Gaylor, E., & Anders, T. F. (2002). Sleep patterns of children with pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 32*(6), 553-561.

Horne, J. A. (1988). *Why We Sleep*. Oxford, UK: Oxford University Press.

Hughes, C. (2002). Executive functions and development: Emerging themes. *Infant and Child Development, 11*(2), 201-209.

Hughes, C., & Graham, A. (2002). Measuring Executive Functions in Childhood: Problems and Solutions? *Child and Adolescent Mental Health, 7*(3), 131-142.

Huttenlocher, P. R. (2002). *Neural plasticity the effects of environment on the development of the cerebral cortex*. Cambridge, MA: Harvard University Press.

Jacob, S. V., & Brouillette, R. T. (2000). Home Monitoring of Sleep and Breathing in Children. *Lung Biology in Health and Disease, 147*, 783-796.

Jankelowitz, L., Reid, K. J., Wolfe, L., Cullina, J., Zee, P. C., & Jain, M. (2005). Cystic fibrosis patients have poor sleep quality despite normal sleep latency and efficiency. *Chest, 127*(5), 1593-1599.

Jenni, O. G., & O'Connor, B. B. (2005). Children's sleep: An interplay between culture and biology. *Pediatrics, 115*(1), 204-216.

Kail, R. (1991). Development of processing speed in childhood and adolescence. *Advances in Child Development and Behavior, 23*, 151-185.

Kail, R., & Hall, L. K. (1999). Sources of developmental change in children's word-problem performance. *Journal of Educational Psychology, 91*(4), 660-668.

Klingberg, T., Vaidya, C. J., Gabrieli, J. D., Moseley, M. E., & Hedehus, M. (1999). Myelination and organization of the frontal white matter in children: a diffusion tensor MRI study. *Neuroreport, 10*(13), 2817-2821.

Korkman, M., Kirk, U., & Kemp, S. (1998). *A developmental neuropsychological assessment*. Austin, TX: The Psychological Corporation.

Kurukulaaratchy, R. J., Fenn, M., Twiselton, R., Matthews, S., & Arshad, S. H. (2002). The prevalence of asthma and wheezing illnesses amongst 10-year-old schoolchildren. *Respiratory Medicine, 96*(3), 163-169.

Kushida, C. A., Chang, A., Gadkary, C., Guilleminault, C., Carrillo, O., & Dement, W. C. (2001). Comparison of actigraphic, polysomnographic, and subjective assessment of sleep parameters in sleep-disordered patients 4. *Sleep Medicine, 2*(5), 389-396.

Kushida, C. A., Littner, M. R., Morgenthaler, T., Alessi, C. A., Bailey, D., Coleman, J., Jr., et al. (2005). Practice parameters for the indications for polysomnography and related procedures: an update for 2005. *Sleep, 28*(4), 499-521.

Lehto, J. E., Juujarvi, P., Kooistra, L., & Pulkkinen, L. (2003). Dimensions of executive functioning: Evidence from children 1. *British Journal of Developmental Psychology, 21*, 59-80.

Levaux, M.-N., Potvin, S., Sepehry, A. A., Sablier, J., Mendrek, A., & Stip, E. (2007). Computerized assessment of cognition in schizophrenia: Promises and pitfalls of CANTAB. *European Psychiatry, 22*(2), 104-115.

Lewin, D. S., & Dahl, R. E. (2002). Preliminary evidence of the neurocognitive sequelae of a sleep restriction protocol in pre-adolescents 1. *Sleep, 25*, A434-A435.

Littner, M., Kushida, C. A., Anderson, M., Bailey, D., Berry, R. B., Davila, D. G., et al. (2003). Practice parameters for the role of actigraphy in the study of sleep and circadian rhythms: An update for 2002 - An American Academy of Sleep Medicine report. *Sleep, 26*(3), 337-341.

Luciana, M. (2003). Practitioner review: Computerized assessment of neuropsychological function in children: Clinical and research applications of the Cambridge Neuropsychological Testing Automated Battery (CANTAB). *Journal of Child Psychology and Psychiatry and Allied Disciplines, 44*(5), 649-663.

Luciana, M., & Nelson, C. A. (1998). The functional emergence of prefrontally-guided working memory systems in four- to eight-year-old children. *Neuropsychologia, 36*(3), 273-293.

Manly, T., Anderson, V., Nimmo-Smith, I., Turner, A., Watson, P., & Robertson, I. H. (2001). The differential assessment of children's attention: The Test of Everyday Attention for Children (TEA-Ch), normative sample and ADHD performance. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 42*(8), 1065-1081.

Manly, T., Robertson, I. H., Anderson, V., & Nimmo-Smith, I. (1999). *The test of everyday attention for children*. Bury St. Edmunds, England: Thames Valley Test Company Limited.

Maquet, P. (2000). Functional neuroimaging of normal human sleep by positron emission tomography 2. *Journal of Sleep Research, 9*(3), 207-231.

Marcus, C. L. (2001). Sleep-disordered Breathing in Children. *Am. J. Respir. Crit. Care Med., 164*(1), 16-30.

Marcus, C. L., Carroll, J. L., Koerner, C. B., Hamer, A., Lutz, J., & Loughlin, G. M. (1994). Determinants of Growth in Children with the Obstructive Sleep-Apnea Syndrome 1. *Journal of Pediatrics, 125*(4), 556-562.

Matthews, A., Ellis, A. E., & Nelson, C. A. (1996). Development of preterm and full-term infant ability on AB, recall memory, transparent Barrier Detour, and Means-End tasks. *Child Development, 67*(6), 2658-2676.

McCann, D., McWhirter, J., Coleman, H., Devall, I., Calvert, M., Wearel, K., et al. (2002). The prevalence and management of asthma in primary-aged schoolchildren in the south of England. *Health Education Research, 17*(2), 181-194.

McKenna, J. J., Loughlin, G. M., Carroll, J. L., & Marcus, C. L. (2000). Cultural Influences on Infant and Childhood Sleep Biology and the Science That Studies It: Toward a More Inclusive Paradigm. In *Sleep and Breathing in Children: A Developmental Approach* (pp. 199-230). New York: Marcel Dekker.

Meijer, A. M., Habekothe, H. T., & van den Wittenboer, G. L. H. (2000). Time in bed, quality of sleep and school functioning of children 1. *Journal of Sleep Research, 9*(2), 145-153.

Milton, B., Whitehead, M., Holland, P., & Hamilton, V. (2004). The social and economic consequences of childhood asthma across the lifecourse: a systematic review. *Child Care Health and Development, 30*(6), 711-728.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: a latent variable analysis. *Cogn Psychol, 41*(1), 49-100.

Moulden, D. J. A., Picton, T. W., Meiran, N., Stuss, D. T., Riera, J. J., & Valdes-Sosa, P. (1997, Jun 16-18). *Event-related potentials when switching attention between task-sets.* Paper presented at the TENNET VIII - Theoretical and Experimental Neuropsychology Conference, Montreal, Canada.

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, 31*(3), 322-330.

Muzur, A., Pace-Schott, E. F., & Hobson, J. A. (2002). The prefrontal cortex in sleep 2. *Trends in Cognitive Sciences, 6*(11), 475-481.

Nakagawa, S. (2004). A farewell to Bonferroni: the problems of low statistical power and publication bias. *Behavioural Ecology, 15*(6), 1044-1045.

Naqvi, S. K., Sotelo, C., Murry, L., & Simakajornboon, N. (2008). Sleep architecture in children and adolescents with cystic fibrosis and the association with severity of lung disease. *Sleep and Breathing, 12*(1), 77-83.

Nilsson, J. P., Soderstrom, M., Karlsson, A. U., Lekander, M., Akerstedt, T., Lindroth, N. E., et al. (2005). Less effective executive functioning after one night's sleep deprivation. *Journal of Sleep Research, 14*(1), 1-6.

Nixon, G. M., Thompson, J. M. D., Han, D. Y., Becroft, D. M., Clark, P. M., Robinson, E., et al. (2008). Short sleep duration in middle childhood: Risk factors and consequences. *Sleep, 31*(1), 71-78.

Norman, D. A., & Shallice, T. (1986). Attention to action: Willed and automatic control of behaviour. In R. J. Davidson, G. E. Schwarts & D. Shapiro (Eds.), *Conciousness and seld-regulation: Advances in research and theory* (Vol. 4, pp. 1-18). New York: Plenum.

Owens, J. (2004). Sleep in children: Cross-cultural perspectives. *Sleep and Biological Rhythms, 2*(3), 165-173.

Owens, J., Maxim, R., Nobile, C., McGuinn, M., & Msall, M. (2000a). Parental and self-report of sleep in children with attention-deficit/hyperactivity disorder. *Archives of Pediatrics & Adolescent Medicine, 154*(6), 549-555.

Owens, J., Spirito, A., & McGuinn, M. (2000b). The Children's Sleep Habits Questionnaire (CSHQ): Psychometric properties of a survey instrument for school-aged children. *Sleep, 23*(8), 1043-1051.

Owens-Stively, J., Frank, N., Smith, A., Hagino, O., Spirito, A., Arrigan, M., et al. (1997). Child temperament, parenting discipline style, and daytime behavior in childhood sleep disorders 1. *Journal of Developmental and Behavioural Pediatrics, 18*(5), 314-321.

Perneger, T. V. (1998). What's wrong with Bonferroni adjustments. *British Medical Journal, 316*(7139), 1236-1238.

Phillips, L. H. (1997). Do "frontal tests" measure executve function?: Issues of assessment and evidence from fluency tests. In P. M. A. Rabbitt (Ed.), *Methodology of frontal and executive function* (pp. 191-210). Hove: Psychology Press.

Pilcher, J. J., & Huffcutt, A. I. (1996). Effects of sleep deprivation on performance: A meta-analysis. *Sleep, 19*(4), 318-326.

Pollak, C. P., Stokes, P. E., & Wagner, D. R. (1998). Direct comparison of two widely used activity recorders. *Sleep, 21*(2), 207-212.

Pollak, C. P., Tryon, W. W., Nagaraja, H., & Dzwonczyk, R. (2001). How accurately does wrist actigraphy identify the states of sleep and wakefulness? *Sleep, 24*(8), 957-965.

Portier, F., Portmann, A., Czernichow, P., Vascaut, L., Devin, E., Benhamou, D., et al. (2000). Evaluation of home versus laboratory polysomnography in the diagnosis of sleep apnea syndrome 1. *American Journal of Respiratory and Critical Care Medicine, 162*(3), 814-818.

Posner, M. I. (2004). Progress in attention research. In *Cognitive Neuroscience of Attention*. New York: Guildford Press.

Posner, M. I., & Petersen, S. E. (1990). The Attention System of the Human Brain. *Annual Review of Neuroscience, 13*, 25-42.

Rabbitt, P. (1997). *Methodology of frontal and executive function*. Hove: Psychology Press.

Randazzo, A. C., Muehlbach, M. J., Schweitzer, P. K., & Walsh, J. K. (1998). Cognitive function following acute sleep restriction in children ages 10-14. *Sleep, 21*(8), 861-868.

Rechtschaffen, A., & Kales, A. (1968). *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects*. Bethesda, Md.: U.S. Dept. of Health, Education, and Welfare.

Redline, S., Tishler, P. V., Schluchter, M., Aylor, J., Clark, K., & Graham, G. (1999). Risk factors for sleep-disordered breathing in children - Associations with obesity, race, and respiratory problems 4. *American Journal of Respiratory and Critical Care Medicine, 159*(5), 1527-1532.

Roder, I., Kroonenberg, P. M., & Boekaerts, M. (2003). Psychosocial functioning and stress-processing of children with asthma in the school context: differences and similarities with children without asthma. *Journal of Asthma, 40*(7), 777-787.

Romine, C., & Reynolds, C. R. (2004). A model of the development of frontal lobe functioning: Findings from a meta-analysis. *Applied Neuropsychology, 12*(4), 190-201.

Ronchetti, R., Villa, M. P., Matricardi, P. M., La Grutta, S., Barreto, M., Pagani, J., et al. (2002). Association of asthma with extra-respiratory symptoms in schoolchildren: Two cross-sectional studies 6 years apart. *Pediatric Allergy and Immunology, 13*(2), 113-118.

Rosen, C. L. (1999). Clinical features of obstructive sleep apnea hypoventilation syndrome in otherwise healthy children. *Pediatric Pulmonology, 27*(6), 403-409.

Rosen, C. L., Storfer-Isser, A., Taylor, H. G., Kirchner, H. L., Emancipator, J. L., & Redline, S. (2004). Increased behavioral morbidity in school-aged children with sleep-disordered breathing. *Pediatrics, 114*(6), 1640-1648.

Sadeh, A., & Acebo, C. (2002). The role of actigraphy in sleep medicine *Sleep Medicine Reviews, 6*(2), 113-124.

Sadeh, A., Alster, J., Urbach, D., & Lavie, P. (1989). Actigraphically based automatic bedtime sleep -wake scoring: Validity and clinical applications. *Journal of Ambulatory Monitoring, 2*, 209-216.

Sadeh, A., Gruber, R., & Raviv, A. (2002). Sleep, neurobehavioral functioning, and behavior problems in school-age children. *Child Development, 73*(2), 405-417.

Sadeh, A., Gruber, R., & Raviv, A. (2003). The effects of sleep restriction and extension on school-age children: What a difference an hour makes 1. *Child Development, 74*(2), 444-455.

Sadeh, A., Hauri, P. J., Kripke, D. F., & Lavie, P. (1995). The Role of Actigraphy in the Evaluation of Sleep Disorders *Sleep, 18*(4), 288-302.

Sadeh, A., Horowitz, I., Wolach-Benodis, L., & Wolach, B. (1998). Sleep and pulmonary function in children with well-controlled, stable asthma. *Sleep, 21*(4), 379-384.

Sadeh, A., Raviv, A., & Gruber, R. (2000). Sleep patterns and sleep disruptions in school-age children. *Developmental Psychology, 36*(3), 291-301.

Sadeh, A., Sharkey, K. M., & Carskadon, M. A. (1994). Activity-based sleep-wake identification - an empirical test of methodological issues. *Sleep, 17*(3), 201-207.

Shallice, T. (1982). Specific impairments of planning. *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences, 298*(1089), 199-209.

Siegel, J. M. (2001). The REM sleep - Memory consolidation hypothesis 35. *Science, 294*(5544), 1058-1063.

Silverstein, M. D., Mair, J. E., Katusic, S. K., Wollan, P. C., O'Connell, E. J., & Yunginger, J. W. (2001). School attendance and school performance: A population-based study of children with asthma. *Journal of Pediatrics, 139*(2), 278-283.

Smedje, H., Broman, J. E., & Hetta, J. (2001). Associations between disturbed sleep and behavioural difficulties in 635 children aged six to eight years: a study based on parents' perceptions. *European Child & Adolescent Psychiatry, 10*(1), 1-9.

Sowell, E. R., Thompson, P. M., Holmes, C. J., Batth, R., Jernigan, T. L., & Toga, A. W. (1999). Localizing age-related changes in brain structure between childhood and adolescence using statistical parametric mapping 1. *Neuroimage, 9*(6), 587-597.

Steenari, M. R., Vuontela, V., Paavonen, E. J., Carlson, S., Fjallberg, M., & Aronen, E. T. (2003). Working memory and sleep in 6-to 13-year-old schoolchildren. *Journal of the American Academy of Child and Adolescent Psychiatry, 42*(1), 85-92.

Stickgold, R. (2000). Inclusive versus exclusive approaches to sleep and dream research *Behavioral and Brain Sciences, 23*(6), 1011-.

Stickgold, R., & Walker, M. P. (2005). Sleep and memory: the ongoing debate. *Sleep, 28*(10), 1225-1227.

Stores, G. (2001). *A clinical guide to sleep disorders in children and adolescents*. Cambridge, UK: Cambridge University Press.

Stores, G., Ellis, A. J., Wiggs, L., Crawford, C., & Thomson, A. (1998). Sleep and psychological disturbance in nocturnal asthma. *Archives of Disease in Childhood, 78*(5), 413-419.

Stores, G., Wiggs, L., & Campling, G. (1998). Sleep disorders and their relationship to psychological disturbance in children with epilepsy. *Child Care, Health and Development, 24*, 5-19.

Stradling, J. R., & Davies, R. J. (2004). Sleep. 1: Obstructive sleep apnoea/hypopnoea syndrome: definitions, epidemiology, and natural history. *Thorax, 59*(1), 73-78.

Strunk, R. C., Sternberg, A. L., Bacharier, L. B., & Szefler, S. J. (2002). Nocturnal awakening caused by asthma in children with mild-to-moderate asthma in the Childhood Asthma Management Program. *Journal of Allergy and Clinical Immunology, 110*(3), 395-403.

Stuss, D. T., & Alexander, M. P. (2000). Executive functions and the frontal lobes: a conceptual view. *Psychological Research-Psychologische Forschung, 63*(3-4), 289-298.

Tabachnick, B. G., & Fidell, L. S. (1996). *Using multivariate statistics* (3rd ed.). New York: Harper Collins.

Thomas, M., Sing, H., Belenky, G., Holcomb, H., Mayberg, H., Dannals, R., et al. (2000). Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. *Journal of Sleep Research, 9*(4), 335-352.

Thomas, M. S. C. (2003). Essay Review: Limits on plasticity. *Journal of Cognition and Development, 4*(1), 99-125.

Tikotzky, L., & Sadeh, A. (2001). Sleep patterns and sleep disruptions in kindergarten children. *Journal of Clinical Child Psychology, 30*(4), 581-591.

Traeger, N., Schultz, B., Pollock, A. N., Mason, T., Marcus, C. L., & Arens, R. (2005). Polysomnographic values in children 2-9 years old: Additional data and review of the literature. *Pediatric Pulmonology, 40*(1), 22-30.

Turner-Warwick, M. (1988). Epidemiology of nocturnal asthma. *American Journal of Medicine, 85*(1B), 6-8.

Urschitz, M. S., Eitner, S., Guenther, A., Eggebrecht, E., Wolff, J., Urschitz-Duprat, P. M., et al. (2004). Habitual snoring, intermittent hypoxia, and impaired behavior in primary school children 2. *Pediatrics, 114*(4), 1041-1048.

Urschitz, M. S., Guenther, A., Eggebrecht, E., Wolff, J., Urschitz-Duprat, P. M., Schlaud, M., et al. (2003a). Snoring, intermittent hypoxia and academic performance in primary school children 4. *American Journal of Respiratory and Critical Care Medicine, 168*(4), 464-468.

Urschitz, M. S., Wolff, J., von Einem, V., Urschitz-Duprat, P. M., Schlaud, M., & Poets, C. F. (2003b). Reference Values for Nocturnal Home Pulse Oximetry During Sleep in Primary School Children. *Chest, 123*(1), 96-101.

Uyan, Z. S., Ozdemir, N., Ersu, R., Akpinar, I., Keskin, S., Cakir, E., et al. (2007). Factors that correlate with sleep oxygenation in children with cystic fibrosis. *Pediatric Pulmonology, 42*(8), 716-722.

Van Dongen, H. P. A., Maislin, G., Mullington, J. M., & Dinges, D. F. (2003). The cumulative cost of additional wakefulness: Dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep, 26*(2), 117-126.

Verhulst, S. L., Schrauwen, N., Haentjens, D., Van Gaal, L., De Backer, W. A., & Desager, K. N. (2007). Reference values for sleep-related respiratory variables in asymptomatic European children and adolescents. *Pediatric Pulmonology, 42*(2), 159-167.

Vertes, R. P., & Siegel, J. M. (2005). Time for the sleep community to take a critical look at the purported role of sleep in memory processing. *Sleep, 28*(10), 1228-1229; discussion 1230-1223.

Villa, M. P., Pagani, J., Lucidi, V., Palamides, S., & Ronchetti, R. (2001). Nocturnal oximetry in infants with cystic fibrosis. *Archives of Disease in Childhood, 84*(1), 50-54.

Walker, M. P., & Stickgold, R. (2006). Sleep, memory, and plasticity. *Annual Review of Psychology, 57*, 139-166.

Watter, S., Geffen, G. M., & Geffen, L. B. (2001). The n-back as a dual-task: P300 morphology under divided attention. *Psychophysiology, 38*(6), 998-1003.

Welsh, M. C., Pennington, B. F., & Groisser, D. B. (1991). A normative-developmental study of executive function: A window on prefrontal function in children. *Developmental Neuropsychology, 7*, 131-149.

Werner, H., Molinari, L., Guyer, C., & Jenni, O. G. (2008). Agreement rates between actigraphy, diary, and questionnaire for children's sleep patterns. *Archives of Pediatrics and Adolescent Medicine, 162*(4), 350-358.

Widenfelt, B., Goedhart, A., Treffers, P. A., & Goodman, R. (2003). Dutch version of the Strengths and Difficulties Questionnaire (SDQ). *European Child & Adolescent Psychiatry, 12*(6), 281-289.

Wiggs, L., Montgomery, P., & Stores, G. (2005). Actigraphic and parent reports of sleep patterns and sleep disorders in children with subtypes of attention-deficit hyperactivity disorder. *Sleep, 28*(11), 1437-1445.

Wolraich, M. L., Lambert, E. W., Bickman, L., Simmons, T., Doffing, M. A., & Worley, K. A. (2004). Assessing the impact of parent and teacher agreement on diagnosing attention-deficit hyperactivity disorder. *Journal of Developmental and Behavioral Pediatrics, 25*(1), 41-47.

Zelazo, P. D., & Muller, U. (2002). Executive function in typical and atypical development. In U. Goswami (Ed.), *Handbook of Childhood Cognitive Development* (pp. 445-469). Oxford: Blackwell.

Zelazo, P. D., Muller, U., Frye, D., & Marcovitch, S. (2003). The development of executive function in early childhood. *Monographs of the Society for Research in Child Development, 68*(3).

Zuckerman, B., Stevenson, J., & Bailey, V. (1987). Sleep Problems in Early-Childhood - Continuities, Predictive Factors, and Behavioral-Correlates 2. *Pediatrics, 80*(5), 664-671.