Sleep Physiology and Executive Function during Chronic Partial Sleep Restriction

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Abstract

Sleep Physiology and Executive Function During Chronic Partial Sleep Restriction
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Introduction: The detrimental effects of sleep deprivation on waking performance are well documented, but questions remain regarding the relationship between sleep physiology and specific domains of cognitive function. Research suggests sleep may also play a role in waking executive functions. However, the existing studies investigating executive functioning have generally been carried out under conditions of total sleep deprivation and only in one instance was the specific relationship between physiological sleep stages and waking executive function investigated. Methods: In this study, N = 137 (22 – 45y, 77m, 60f) participants completed a chronic sleep restriction protocol of four hours time in bed for sleep for five consecutive nights. Following sleep restriction, the Hayling and Brixton tests of executive functioning (HBT) were administered. Sleep variables, recorded the night prior to test administration, were regressed on the HBT measures. In a secondary analysis, the performance of a small group of control participants was compared to the group of sleep restricted participants using t-tests. Results: The results supported our hypothesis that slow wave sleep would be the best predictor of subsequent performance on tests of executive function, though the amount of variability accounted for was less than 10%. Additionally, the performance of sleep restricted individuals was relatively worse than individuals obtaining normal sleep on certain measures of cognitive functioning, including attention and certain aspects of executive function. Discussion: These findings indicate that having more slow wave sleep during sleep restriction predicts fewer errors, shorter response latencies, and better overall performance on tests of executive function. Implications are discussed for clinical neuropsychological practice with respect to the potential impact of sleep loss on neuropsychological testing.

Introduction

According to a survey of Americans' sleeping habits conducted by the National Sleep Foundation (NSF "Sleep in America", 2002), a significant proportion of adults (39%) sleep less than seven hours per night during the work week, and more than two-thirds (68%) sleep less than eight hours per night. Thus, as the "work-day" becomes the "work-night", many are relinquishing their time for sleep to the demands of work. It is argued here that this behavior likely costs them the very performance capability they often require to cope effectively with those work demands. It seems clear that even one night of sleep loss can significantly impact the quality of one's work performance, especially in more complex, thought driven working environments, or those which require a high level of performance on multiple tasks.

Researchers in fields ranging from behavioral genetics to cognitive psychology have demonstrated important relationships between sleep and waking functions (See Pilcher & Huffcutt, 1996; Reppert & Weaver, 2001; Pace-Schott & Hobson, 2002 for reviews). A brief overview of this research follows to illustrate how the loss of sleep, even in otherwise healthy individuals, can negatively impact important waking cognitive functions – including those associated with frontal lobe and executive functions. It also lays the groundwork for a neuropsychological approach to investigating the role of different aspects of sleep in the more specific aspects of cognitive functions, such as those mentioned at the outset. This study will investigate the relationship between REM sleep and slow wave sleep (SWS), and certain executive abilities including creative thinking, cognitive flexibility, rule attainment, response initiation and response inhibition.

Executive Function

The term executive function has been used to refer to multiple cognitive processes such as the intentional redirection of attention, the inhibition/regulation of

behavioral or emotional responses, cognitive or motor planning, the initiation and execution of strategies, rule apperception, and cognitive flexibility (Lezak, 1995). These abilities are essential for optimum performance in environments which require sustained multi-tasking, organization, and problem solving. Even at the more basic level of every-day quality of life, executive functions are critical. In her widely utilized compendium of neuropsychological tests, Muriel Lezak notes that if executive functions are intact, an individual may sustain serious cognitive loss, yet still have the capacity to function independently and can continue to be a productive member of society (Lezak, 1995).

There has been little disagreement that the primary substrate for these diverse capabilities is the prefrontal cortex (PFC), as patients with PFC lesions often demonstrate problems with planning, behavioral initiation, rule apperception, organization, cognitive flexibility and often show perseverative tendencies, attention and memory problems, and deficits in judgment and reasoning (see Buschbaum et al, 2005 for a meta-analysis). Importantly however, some researchers (see Goldberg and Bougakov, 2005) warn against the interchangeable use of the terms “executive function” and “frontal lobe function”, noting that executive function is also supported by other cortical and subcortical areas such as the anterior cingulate cortex, basal ganglia, the dorsomedial thalamic nucleus, cerebellum and the ventral mesencephalon. Their definition of executive function, which reflects the involvement of these areas, includes goal setting, cognitive tool selection, cognitive switching and flexibility, and self-evaluation of the execution and outcome of cognitive planning.

For the present study, a subset of executive functions will be assessed using Burgess’ and Shalice’s (1997) Hayling Sentence Completion Test and Brixton Spatial Anticipation Test. The Hayling will be administered to assess creative/divergent thinking (or the ability to generate novel solutions to problems), and response initiation and inhibition. Cognitive flexibility, or the ability to shift cognitive set, will be evaluated using

The Brixton Spatial Anticipation Test. These tests have not enjoyed widespread use in research protocols or clinical settings. However, as will be discussed later, their combination offers an ecologically valid assessment of executive functions (Odhuba , et al, 2005) and may be seen as a complement to those studies employing more frequently used neuropsychological tests of executive function such as The Wisconsin Card Sorting Test (WCST). These tests also have the advantage of being amenable to bedside administration during a short window of time while still yielding valuable information about divergent thinking, cognitive flexibility, response initiation and inhibition, and rule attainment.

In the following review, existing research on the neurophysiology of sleep and executive function is reviewed, as well as studies which have already shed some light on the relationships between this sleep and waking cognitive processes, including executive function. This body of research has raised important questions about the role of sleep in the restoration of waking executive abilities. However, the role of particular sleep stages in the waking ability to perform complex executive level tasks is still largely unknown. To help bridge this gap, this study will investigate the relationships between specific sleep states and consequent performance on the Hayling and Brixton tests. Additionally, while many previous studies have used total sleep deprivation (TSD) protocols to probe the effects of sleep loss on cognitive function, this study is based on a chronic partial sleep restriction (CPSR) paradigm, in which participants are allowed an abbreviated sleep period every night over several nights. The degree to which these research approaches induce comparable degrees of sleep debt is not fully known, though some research has suggested that they are equivalent in some respects (See Van Dongen, et al., 2003). Overall, this study represents a departure from previous approaches to understanding the relationship between sleep and cognitive function in that the focus here is on

executive functions, and the specific relationships between sleep stages and subsequent waking executive functions in healthy, sleep restricted adults.

Sleep Physiology

Human sleep and wake cycles have been qualitatively and quantitatively conceptualized using the two-process model of sleep-wake regulation (Borbely, 1982). According to the two-process model, the timing and structure of sleep is the product of a non-linear interaction between homeostatic and circadian processes – processes S and C, respectively (Borbely, 1982).

Since the introduction of Rechtschaffen and Kales' (1962) standardized criteria for staging sleep, sleep architecture, or the electrophysiological correlates of sleep physiology, has been reduced to five primary stages based on characteristic polysomnographic features. Stage 1 sleep contains vertex sharp-waves and increased alpha frequency (8 - 12hz) activity with respect to waking. Stage 2 sleep is marked by decreased alpha and the emergence of k-complex wave-forms and sleep spindles; Stage 3 slow wave sleep (SWS) is marked by the appearance of delta waves (.5 - 4hz); Stage 4 SWS, is characterized by the presence of these delta waves in at least 50% of the sleep EEG. Rapid eye movement (REM) sleep, which follows SWS in the normal temporal progression of a sleep episode, and which is characterized by a low-amplitude, mixed-frequency EEG signal (similar to waking EEG), an atonic EMG signal, and rapid ocular saccades in phasic REM or little to no ocular activity during tonic REM.

The alternation of REM and NREM during sleep follows an ultradian rhythmicity of approximately 90 minutes. It has been suggested that this ultradian alternation is the result of interplay between aminergic and cholinergic neurons of the mesopontine junction (McCarley and Hobson, 1988). While awake, the pontine aminergic system is active and inhibits the pontine cholinergic system, which is responsible for initiating REM sleep. During NREM sleep, this aminergic inhibition subsides and cholinergic excitation increases until REM sleep onset, where aminergic inhibition of REM terminates and

cholinergic excitability reaches a peak. During REM, other outputs, most notably motor outputs, are inhibited (McCarley and Hobson, 1988; Pace-Schott and Hobson, 2002).[1] A revised version of this model allows for intermediate inputs into this REM-on/REM-off system which may explain the changes in sleep physiology in response to various drugs and disorders (see Pace-Schott and Hobson, 2002 for a review).

The interplay between thalamic and cortical neurons generates the characteristic slow wave forms of stages 3 and 4 sleep (Steriade et al. 1993). These slow waves appear to be generated by intrinsic oscillating properties of certain thalamic neurons or by cortical input to inhibitory thalamic interneurons. REM sleep activity emerges from an increase in the firing rates of a distributed network of neurons at the reticular, thalamocortical and cortical levels. Phasic REM-sleep potentials occur sequentially in the pons, propogating along projections to the thalamic lateral geniculate body, and the occipital cortex, producing the characteristic ponto-geniculo-occipital (PGO) waves and possibly representing the neural substrates of dreamed visual phenomena. This pattern of activation is the result of the tonic disinhibition and phasic excitation of burst cells in the lateral pontomesencephalic tegmentum (See Hobson & Stickgold, 2000 for a detailed review).

Total Sleep Deprivation versus Chronic Partial Sleep Restriction

Many studies have investigated the effects of total sleep deprivation, but few have investigated cognitive functioning after chronic partial sleep restriction. The increasingly common practice of sleeping two or more hours less than the recommended 8h per night for multiple consecutive nights (i.e. chronic partial sleep deprivation) has been shown to produce some performance impairments similar to those seen after contiguous total sleep deprivation. Van Dongen and colleagues (2003) have illustrated

[1] A revised version of this model allows for intermediate inputs into this REM-on/REM-off system which may explain the changes in sleep physiology in response to various drugs and disorders (see Pace-Schott and Hobson, 2002 for a review).

this by comparing the performance of healthy individuals during 88h of total sleep deprivation (TSD), with that of individuals sleeping 4h, 6h, or 8h per night for multiple consecutive nights tests of sustained attention, visuospatial tracking and transcoding, and serial addition and subtraction. Significant differences were demonstrated in the rate of change across days among the four groups on all performance measures. Individuals in the TSD group demonstrated the poorest performance on all tests, while those in chronic sleep restriction conditions demonstrating increasingly better performance respectively. Interestingly, performance deficits on a psychomotor vigilance test (PVT) measuring sustained attention (Dinges & Powell, 1985) showed a near-linear relationship with the cumulative amount of excess-wakefulness, which was calculated as the time awake in excess of an estimated critical period of wakefulness of approximately 16h. In other words, each additional hour of wakefulness beyond this critical amount, was associated with an increasing difficulty in sustaining attention.

Thus, the hypothesis that chronic partial sleep restriction is associated with performance deficits similar to that of total sleep deprivation was supported with respect to tasks involving sustained attention and insofar as it is the number of cumulative excess hours awake that is the best predictor of neurobehavioral performance. However, this hypothesis has not been extended to an investigation of how executive abilities are affected by chronic partial sleep restriction. In addition, few studies have assessed the role of sleep physiology in the performance of executive-type tasks.

Changes in waking performance after sleep deprivation have been reported on extensively in studies of real-world sleep deprivation and within experimental settings (Mitler, et al, 1988; Dinges and Kribbs, 1991; Dement, 1994; Belenky, et al, 1994; Baldwin and Daugherty, 2004; Lockley, et al., 2004). However, few studies have investigated the precise nature of the relationship between sleep physiology and waking cognitive functioning in the laboratory (i.e. Clark, et al., 1998; Stickgold, 2001; Finelli, et

al., 2001; Anderson and Horne, 2003; Van Dongen, et al, 2004; Durmer and Dinges, 2005). What follows is a brief summary of this emerging body of research. These studies have implications for understanding both the impact of sleep loss on neurocognitive functioning as well as for understanding functions of different aspects of sleep physiology.

Sleep and Cognitive Function

While several researchers have postulated theories of how sleep and waking neurocognitive functions are related, Alan Hobson and colleagues have put forth one of the most comprehensive, yet parsimonious models for how these states are related. In their review of the cognitive neuroscience of sleep, Hobson and Pace-Schott (2002) approach propose three cardinal states of consciousness - Wake, Non-REM sleep, and REM sleep. Briefly, at the cognitive level, wake is responsible for the acquisition of information, non-REM is responsible for the reiteration of information, and REM is responsible for the integration of information.

It is important to note here that the division of sleep into Non-REM and REM, or stages 1 – 4 and REM, remains somewhat arbitrary and there continues to be some debate over how sleep-related EEG activity should be characterized. Certainly the division of consciousness into wake, non-REM, and REM sleep is artificial, but a full exploration of these issues is beyond the scope of this review (for more complete reviews, see Carskadon and Rechtschaffen, 1995; Stanley, 1996). Nonetheless, in the absence of a more appropriate, consensus standard, it appears to make biological and practical sense to divide sleep in this way. Not only is there a great deal of research demonstrating the double dissociation with regard to the physiological characteristics of these states, but it has been shown that Non-REM, particularly slow wave sleep (stages 3 and 4) and REM-sleep likely have very different relationships with waking function.

Non-REM Sleep

Non-REM sleep actually encompasses very different physiological states ranging from sleep onset (stages 1 and 2) to the deepest stages of sleep (stages 3 and 4). Slow wave sleep (SWS) is of particular interest, as it is widely believed to serve imperative

growth-related and restorative functions (Born, et al., 1988; Sassin et al., 1969). In addition, a number of studies have shown that SWS is closely correlated with learning and memory functioning (for a review see Hobson & Pace-Schott, 2002) and potentially for the restoration of frontally mediated executive functions (Harrison and Horne, 2000; Finelli, et al., 2001 – both reviewed later).

Destexhe and Sejnowski (2004) summarize work from animal and human studies which provides strong evidence that SWS may operate to prune and/or strengthen newly acquired memories via complex interactions between the thalamus, cortex, and hippocampus. In addition, Hobson and Pace-Schott (2002) have proposed that the rapid spontaneous firing of cortical neuronal populations during SWS may be related to memory consolidation and learning processes. Experimentally induced spindle activity (similar to the naturally occurring sleep spindles seen primarily in stage 2 sleep) produces persistent changes in neuronal responsiveness thought to reflect long-term potentiation (Steriade, 1999; Steriade, 2000). More recently, SWS has been shown to increase following a rotational learning task and positively correlated with better performance subsequent to sleep (Huber et al. 2004), suggesting a role for SWS in procedural learning.

REM Sleep

REM sleep has also been associated with memory and learning functions. Selective deprivation of REM sleep has been demonstrated to produce learning decrements, particularly with respect to procedural tasks (Hobson and Pace-Schott, 2002; Stickgold et al., 2000; Stickgold, et al., 2001; Gais, et al. 2000; Karni, et al., 1994). For instance, Stickgold et al. (2001) found that REM may function as a procedural learning enhancement state which consolidates and elaborates newly learned motor and cognitive routines, such as learning to play Tetris. Importantly, the relationship between

REM sleep and the consolidation of procedural memory appears to be dependent upon the length of time between learning, the subsequent REM episode, and the time of recall (Smith, 1985).

Despite a strong evidence base suggesting that procedural memory consolidation is one function of REM sleep, this is not the only function which has been proposed for REM sleep and it is not established that REM sleep is necessary for this type of memory consolidation. In fact it is well known that consolidation can occur in the absence of REM sleep (Stickgold, 2001). Also, while REM sleep has been associated with the consolidation of procedural memory in several studies, there are fewer examples of REM sleep impacting on declarative memory (Smith, 1996). REM sleep may serve other functions as well, particularly with regard to early brain development. For example, the developmental wiring of binocular cells in visual cortex (Frank et al., 2001; Shaffery et al., 1999), and the development of problem solving skills (Smith, 1993) have also been posited as potential functions of REM sleep.

Beyond the consolidation of procedural memory, and the facilitation of normal development, REM sleep seems to be involved in either consolidating or elaborating other kinds of newly acquired information. Increases in the amount of REM sleep following learning have been reported for complex logic games (Smith, 1993), foreign languages (Dekoninck et al., 1989), and after studying (Smith and Lapp, 1986). Stickgold (2001) suggests that these findings indicate that REM sleep may affect neocortical networks. The role for REM sleep in the acquisition and enhancement of these cognitive functions implies that REM may even support executive functions with regard to problem solving situations and perceptually mediated executive functions. However, based on existing research, it seems SWS plays a more substantial role than REM sleep in the restoration of many executive functions.

Neuroimaging of Sleep and Cognitive Performance

A different approach to understanding relationships between sleep physiology and waking cognitive function is by investigating the effects of sleep loss on waking brain activation and cognitive performance. Neuroimaging studies of sleep deprived individuals have implicated various brain areas which may underlie changes in waking cognitive performance during sleep deprivation (Portus, et al, 1998; Wu, et al, 1991; Thomas, et al, 2000; Drummond and Brown, 2001; Drummond, et al, 2005). Specifically, there has been convergence on certain brain areas, including the prefrontal cortex (PFC), thalamus and posterior parietal lobules, which consistently exhibit decreases in activity across studies (Drummond and Brown, 2001; Thomas, et al, 2000). Taken together, these decreases in activity may explain the decrements in cognitive performance observed following sleep deprivation. Executive functions, in particular would appear to be particularly susceptible to impairment following sleep loss.

Gallassi and colleagues (1996) identified the progression of neuropsychological decline in patients with fatal familial insomnia as following a path whereby there is early impairment of attention and vigilance followed by deficits of working memory, eventual impairment of temporal ordering ability and finally a progressive dream-like state with features of a demented state. Furthermore, while all patients in their study suffered neuronal loss at the thalamic level, pathology results revealed two patients experienced substantial cerebral degeneration as well. In these patients, categorical thinking and verbal fluency were also impaired.

In one of the earliest fMRI studies of cerebral response to cognitive demands during total sleep deprivation, Portus and colleagues (1998) investigated the effects of varying levels of arousal on an attention task. To manipulate arousal levels, the investigators had subjects perform the attention task during one of three conditions: An

unaltered period of high arousal with no sleep deprivation and after the administration of caffeine; A normal arousal condition without sleep deprivation; And a low arousal condition following 24h total sleep deprivation. The attentional task produced consistent activation within the intraparietal sulcus and the most anterior portion of the middle frontal gyrus. The authors hypothesized that a change in activation (BOLD response) would occur in the thalamus as an expression of the interaction between the cortical attentional and subcortical arousal systems. Results demonstrated that the better performance on the attentional task was, in fact, associated with increased activation in the thalamus across conditions and that the highest level of attention-related thalamic activation occurred only in sleep deprived individuals, possibly acting as a compensatory mechanism for decreased PFC activation.

Thomas and colleagues (2000) employed positron emission tomography (PET), measuring cerebral metabolic rate for glucose (CMRglu), to investigate the effect of 24h total sleep deprivation on the performance of a serial addition/subtraction task. Impaired alertness and cognitive performance secondary to sleep deprivation were associated with an 8% reduction in whole brain metabolic rate. Absolute regional CMRglu was decreased bilaterally throughout the PFC including, in the posterior parietal lobules, in the dorsal and ventral thalamus, in the parahippocampal gyri, in areas of the temporal lobes, and the cerebellar hemispheres and vermis. Significantly decreased regional glucose metabolism, relative to the absolute global decrease of 8%, was demonstrated bilaterally in the PFC (including the dorsal anterior portions of the cingulate gyrus), thalamus, middle and inferior temporal gyri, medial temporal cortex including the right fusiform and parahippocampal gyri, vermis, and in a small area in the right ventral cerebellar hemisphere. These findings, particularly the decreased activation in the PFC and thalamus, are consistent with other studies and may explain the association

between perseverative tendencies and slow wave activity in the left PFC (Anderson and Horne, 2003).

Even on simpler tasks such as novelty detection, a process mediated by frontal brain areas such as the anterior cingulate cortex and supplemental motor area, sleep deprived individuals perform at levels *similar to those of patients with frontal lobe lesions* (Gosselin, et al., 2005). The authors demonstrated that the novel P300 component was reduced over the frontal scalp after 36h of total sleep deprivation. They conclude that since theirs was a simple signal detection task (oddball paradigm), that decrements performance on frontal lobe functioning tasks is not limited to cases in which highly complicated, novel, and cognitively demanding tasks are used. Instead, their findings suggest that even basic, frontally mediated response initiation is likely to be adversely affected by sleep loss. The authors point out that their findings were consistent with observations of patients with frontal lobe injuries, however they admit that potential moderating or mediating effects of sensory variables (i.e. the N100 component) were not sufficiently addressed in their study. Nonetheless, these results also seem to support the hypothesis that set-shifting and rule apperception, based on environmental cues, may be impaired during periods of sleep deprivation since it is often the detection of a pattern change that alerts an individual that a rule has changed and a shift in set is necessary (see discussion of Brixton test below).

Across three separate fMRI studies, Drummond and colleagues investigated the effects of sleep deprivation on cerebral responses to various cognitive tasks (Drummond, et al, 1999; 2000; 2001). These studies demonstrated impairment in verbal learning after a period of 35h total sleep deprivation. Interestingly, lower levels of impairment were correlated with greater activation in the bilateral parietal lobes (including the language areas of the left inferior parietal lobe) suggesting a possible compensatory response in this area to the effects of sleep deprivation. Consistent with

Thomas et al's (2000) findings, Drummond noted that better performance on an arithmetic test following TSD was not correlated with any difference in brain activation – suggesting that such a compensatory cerebral response is absent for this type of task. Not surprisingly, greater activation was also found in the bilateral PFC, bilateral parietal lobes, and the cingulate gyrus with better performance on combined verbal learning/arithmetic tests. Thus, changes in regional activation during SD may reflect the brain's compensatory response to task-specific demands creating a more complicated picture of how sleep loss affects cognitive functioning. The involvement of the left inferior parietal lobe in short-term verbal memory storage (Jonides, et al., 1997) and its increased relative activation during TSD suggest that this area is likely coming on-line in a compensatory role during periods of sleep deprivation. The switch from temporal to parietal involvement for verbal learning is less efficient, which may explain the performance decrement associated with that task (Drummond, 2000).

As mentioned, Drummond's results complicate the picture for identifying correlations between sleep and executive function, since the brain may be compensating in some areas rather than others, selectively enhancing functions normally served by susceptible brain areas. However, these findings may not suggest a compensatory process at all, but rather the ability of certain individuals to sustain higher levels of cognitive performance during sleep loss due to some advantageous phenotype. Importantly however, this study provides further evidence that executive performance may be impacted by sleep loss based upon the changes in activation seen in bilateral PFC, parietal lobes and anterior cingulate.

As neuroimaging data accumulate, it appears increasingly clear the most common brain regions exhibiting changes in response to sleep loss include the thalamus, bilateral parietal lobes, cingulate cortex, and most importantly for the present study, the prefrontal cortex. These changes range from decreased activation to

increased and perhaps compensatory activation during waking cognitive performance. Consequently, a review of the neurocognitive and neurobehavioral correlates of these areas may be useful in reconciling research from functional neuroimaging and experimental research demonstrating performance decrements associated with sleep loss with the theoretical basis for this study. The employment of neuropsychological testing may offer some clarification with regard to the neurocognitive consequences of observed changes in brain activity following sleep deprivation. However, it is important to first consider what changes should be expected given the observed cerebral response to sleep loss.

Functional Correlates of Brain Areas Impacted by Sleep Loss

Clearly, any associations between sleep and executive function will depend on the effects of sleep on areas supporting executive function. However, such associations may also be explained by sleep related activity supporting upstream cognitive processes which, in turn, support executive function. To minimize the likelihood of this becoming a problem for interpreting the results of this study, tests of both executive and more "basic" cognitive functions have been included. These are discussed later in further detail.

However, a basic understanding of the cognitive correlates of areas of the thalamus, parietal lobes, temporal lobes, and PFC affected by sleep loss is needed to place the current study in its proper context. This context is comprised of dynamic interactions between lower, more basic cognitive functions (i.e. attention, motor function) associated largely with subcortical areas of the brain, and higher, more complex functions such as cognitive flexibility, rule attainment, and behavioral inhibition which are typically associated with neocortical areas – all of which are affected by sleep deprivation.

Subcortical Areas

The thalamus is the main sensory relay station for incoming information, making it critical for even the most basic neurobehavioral output. The dorsal and ventral thalami relay and modulate sensory information traveling to and from the PFC, particularly through the nucleus medialis dorsalis (Damasio and Anderson 2003). Generally, there is increased thalamic activation during TSD (Drummond, et al., 2000). Drummond and colleagues propose this happens through increased modulation of sensory information to the cortex. As cognitive demands are introduced, the thalamus has been shown to become more or less activated, presumably based on the nature of the task involved.

As might be expected, thalamic activation increases in response to increases in attentional demand during sleep deprivation (Portas, et al, 1998). However, performance on a serial addition and subtraction task was shown to be associated with decreased thalamic activation during total sleep deprivation of similar duration (Thomas, et al., 2003). One hypothesis for why the thalamus exhibits this pattern of activation is that it serves in a compensatory capacity, filling in for functions normally served by other brain areas (such as the PFC) which are perhaps more susceptible to sleep loss. The decrease in thalamic activation during the serial addition/subtraction task implies this is not the case for all cognitive processes.

This has important implications for predictions about the relationship between sleep and executive functioning. For instance, target detection could easily be considered as one possible mediating variable for any relationship between sleep and various executive functions. More specifically, decreased thalamic activation associated with impaired target detection might be expected to negatively impact performance on tasks requiring the detection of stimuli for the purpose of some further cognitive manipulation (i.e. rule attainment, set shifting, response initiation). Impaired performance on executive tasks measuring the aforementioned variables may thus be explained by reduced modulation between sensory and executive areas.

Cortical Areas

With regard to cortical functions, the superior parietal lobule (BA 7) has been linked to visuomotor coordination and spatial/motor area integration. The parietal operculum (BA 40), which extends anteriorly to the inferior frontal lobes, is activated during activities involving somatosensory stimulation, texture discrimination, as well as other motor tasks involving sensory feedback.

Diminished activation in the parietal operculum following sleep loss might explain performance decrements seen on procedural tasks which draw on procedural abilities, particularly visuomotor integration such as the Rey-Osterrieth Complex Figure Test (see Smith, 1996 for a review of other procedural tasks which are sensitive to sleep deprivation). Interestingly, damage to the inferior-posterior parietal lobules has also been implicated in agnosia for hemiparesis (Bisach, et al., 1986), suggesting sleep loss may not only lead to decrements in sensorimotor functioning, but also to a decreased insight into such decrements. These areas are not presumed to play a significant role in executive function per se, but obviously, impairments in these domains would likely impact performance on any test which tap somatosensory functioning or which involve some degree of visuomotor integration. The specific relationship between sleep physiology and parietal lobe functioning is not entirely clear, and the executive battery in this study is not presumed to involve these abilities. However, the emerging research into the effects of sleep deprivation on cognitive processes such as procedural learning and memory will hopefully illuminate the nature of this relationship

Frontal Areas

Brodmann's area 8 of the prefrontal cortex includes the frontal eye fields. This area shows decreased activation during sleep deprivation and has been associated with the management of uncertainty in decision making (Deppe, et al, 2005). The increase in subjective uncertainty was associated with increased activation in this area suggesting that decreased activation may be related to an impaired ability to manage ambiguity when faced with a decision.

In a single photon emission computed tomography (SPECT) study of the individuals performing on the WCST, regional cerebral blood flow in granular polar and frontopolar areas (BA's 9 and 10) was elevated during WCST relative to rest state and

positively correlated with the number of categories completed (Yang, et al, 2003). While they did not investigate the effects of sleep deprivation, their results suggest that the granular polar and frontopolar areas are important for set shifting and set maintenance and that a decrease in activation in these areas such as that occurring subsequent to sleep loss may lead to fewer categories completed in tests involving rule attainment and cognitive flexibility. In addition, activity in the middle frontal area, granular polar area and frontopolar area (BA's 46, 9, and 10 respectively) were negatively correlated with perseverative errors (Yang, et al, 2003), suggesting a potential role for these structures in cognitive flexibility. The dorsal and ventral anterior cingulate gyri (BA 32), which Thomas et al. (2000) found to have decreased activation after total sleep deprivation, have been associated with an indifference to stimuli or akinetic states in lesion studies (Zaidel, et al, 2003). A state of reduced attention and responsiveness to environmental stimuli may contribute to decrements response latency often observed during sleep deprivation. The orbital gyri, gyrus rectus, and rostral portion of the superior frontal gyrus compose BA 11, which is thought to play a key role in olfaction, emotion, behavioral inhibition, and the representation of the reward and punishment value of primary reinforcing stimuli (see Kringelbach and Rolls, 2004 for a review). A decrease in activation in the superior frontal region might, among other effects, manifest then with a lack of inhibition, and errors in judgment.

The role of frontal areas in executive functioning is widely accepted and research such as that discussed above allows a greater degree of specification for predictions about the kinds of problems which may be associated with sleep loss. Specifically, the cognitive correlates of those areas of the frontal lobes discussed above seems to suggest that sleep loss may be associated with decrements in judgment, response inhibition, cognitive flexibility, and rule attainment. This hypothesis is supported in the

following section, which will introduce the growing body of research describing the known relationships between sleep deprivation and executive function.

Sleep and Executive Function

While the preponderance of evidence points to a role for both SWS and REM sleep in supporting learning as well as explicit and procedural memory consolidation. Research has also suggested that sleep loss may also lead to decrements in executive function. Specifically, positive associations have been reported between SWS and changes in activation in brain areas thought to support executive functions. These studies have been scarce, but seem to point to SWS as the primary sleep state involved in restoring certain executive functions.

One such study by Finelli and colleagues (2001) found a significant increase in low-frequency (i.e. delta) power in frontal areas during recovery sleep after 40h of total sleep deprivation. They posited this increase may be due to greater 'recovery need' of the frontal heteromodal association areas of the cortex, though no neuropsychological testing was employed in their study to substantiate this claim. Their findings are important nonetheless, since they suggest an increased need for restoration in the frontal lobes points to a particular susceptibility of these areas to sleep loss.

This has been supported by evidence from Anderson and Horne (2003), who reported that the amount of slow-wave activity (0.5 - 1hz range) in the left frontal EEG during sleep was significantly associated with performance on tests sensitive to left PFC functioning in older adults. They employed several commonly used measures of executive function including the Wisconsin Card Sorting Test (WCST), the Tower of London (TOL), and a verbal fluency measure. Left frontal slow-wave activity (in the .5-1 Hz range) was significantly and negatively correlated with perseverative errors on a test of cognitive flexibility (WCST) and positively correlated with completion time on a non-verbal planning task (TOL). Verbal fluency was only associated with greater left frontal slow-wave activity among individuals with tertiary education. A ten minute sustained

attention task was not significantly correlated with slow left frontal activity during sleep. Anderson and Horne's study strongly suggest that SWS is important for certain executive functions such as planning, cognitive flexibility, and word generation to command. Unfortunately, their results may not be entirely generalizable, as their sample represented only a narrow subset of the population (aged 61 – 75 years).

However, despite limitations to these two studies, further evidence from neuroimaging research and neuropsychological investigations of sleep-wake relationships provide further basis for the argument that sleep, and slow wave sleep in particular, supports executive function. Evidence suggesting a positive correlation between sleep and the performance of executive tasks, has emerged largely from studies of sleep deprivation. As will be discussed below, extended periods of sleep deprivation or restricted sleep tend to lead to decreased activation in brain areas crucial for executive function and decreased performance on tests sensitive to executive abilities.

Sleep Deprivation and Executive Function

As may be deduced from the above discussion, sleep loss is also associated with changes in brain function that may be expected to impact executive function, perhaps in some domains to a level similar to that of patients with frontal lobe lesions (i.e. Gosselin, et al., 2005). While the literature is still unclear as to the persistence, severity and/or consistency of executive deficits in healthy adults experiencing chronic sleep loss, it is clear that many of the neurological structures involved in executive functions, including the prefrontal cortex, anterior cingulate cortex, and dorsomedial thalamus, exhibit changes in activation following periods of extended wakefulness.

In one of the earliest studies in this area, Horne (1988) demonstrated significant impairments in a construct he termed “divergent thinking”, in students deprived of sleep for 32 consecutive hours. Participants completed tests of verbal and figural flexibility and creativity, all of which showed significant impairment on some or all dependent measures, and showed a significantly increased perseverative tendency relative to non-SD subjects. Horne reported that divergent thinking, as well as many of the other executive functioning variables assessed, including planning time, perseverative tendency, and verbal fluency were impaired. However, Horne did not assess some of the supportive functions, such as basic psychomotor response speed, visual attention or basic concentration, which might explain these results more parsimoniously. Regardless of its limitations, Horne’s study set off a debate over the role of sleep for executive function which has yet to be settled.

Wimmer and colleagues (1992) attempted to build on Horne’s (1988) findings by comparing sleep deprived (TSD) versus non-sleep deprived subjects on the figural form of the Torrance Test of Creative Thinking as well as on measures of attention, working memory, processing speed, set shifting, auditory discrimination, and visual recognition.

Wimmer found that sleep deprivation was associated with decrements in performance on tests of creative thinking, processing speed, set shifting and visual recognition.

Recently, Nilsson and others (2005) compared a small sample (N=22) of sleep deprived (32h TSD) and non-sleep deprived volunteers on an executive measure of supervisory control known as the Six Elements Test, which involves performing story-telling, simple arithmetic calculation, and object naming tasks, while continually monitoring their own adherence to a set of rules. In addition, they administered a serial reaction time test and the Claeson-Dahl test of verbal working memory and episodic memory. The authors found significant differences between sleep deprived and control subjects on the Six Elements Test (SET), but importantly no differences on measures of reaction time or working memory. As a result, the authors point out; the effects of sleep loss on executive functioning cannot be fully explained by deficits in vigilance or working memory subsystems. The differences between groups were presumed unlikely to be explained in terms of motivation (i.e. comparing a dull monotonous task such as reaction time to a novel and engaging task such as the SET) or differences in task difficulty, since the investigators used a simplified version of the SET, designed for individuals with low IQ as a means of modifying the task difficulty between conditions, which led to no significant differences. Their construct of supervisory control may, within the context of the present study, be likened to a conglomerate of response initiation, response suppression, rule attainment (or the ability to establish mental set), and cognitive flexibility (the ability to shift mental set).

Harrison and Horne (2000) review a study of business students who underwent prolonged total sleep deprivation and attempted to perform a complex game involving the development marketing strategies in increasingly difficult circumstances. In this case, sleep deprivation was associated with a decrement in the creativity of play, as sleep deprived players continued to employ previously successful strategies in the face

of negative feedback, while non sleep deprived individuals were more innovative and, thus, more successful.

Surprisingly, Binks and colleagues (1999), who administered several tests of executive functioning to individuals after 32-36 hours of continuous wakefulness, including The Controlled Oral Word Association Test, WCST, a word fluency test, The Booklet Form of the Category Test, the Stroop test, and the adult version of the Paced Auditory Serial Addition Test, found no significant differences on any outcome measure. Although sleep deprived participants reported "feeling" that their performance was impaired, the hypothesis that 32-36h without sleep would adversely affect executive functioning was not supported in their study. This study clearly raises questions about the existence of a relationship between sleep and executive processes. However, it is important to not that several factors which are known to influence performance during sleep deprivation were not controlled for in Binks' study including prior sleep history, physical activity, and light exposure. Sleep history was subjectively assessed and individuals were permitted to walk around the ward during deprivation period, possibly introducing differing amounts of light exposure and uneven levels of physical activity between groups. Also, in one of the few studies of executive function during chronic partial sleep restriction (defined by the investigators as sleep experimentally restricted by 40% of the sleeper's habitual sleep time for 5 consecutive nights), only a non-significant trend for increased perseverative tendency on the WCST was found (Herscovitch, 1980).

Studies investigating relationships between sleep and waking cognitive performance in both experimental and "real world" settings have continued to present ambiguities which have been difficult to reconcile due to differing methodologies and operational definitions. A case in point, Leung and Becker (1992) published a review paper investigating whether the sleep deprivation significantly impaired house staff

performance. They found that the current data (in 1992) was inconclusive because, at that time, different methodologies in assessing performance, arbitrary definitions of sleep deprived and rested states, and the frequent grouping of acute and chronic sleep deprivation rendered questions about “real world” cognitive functioning largely inaccessible. Even studies with similar methodologies (i.e. Horne, 1988, and Wimmer, 1992) have produced different outcomes with respect to sleep and executive function.

Limitations of Previous Research

Overall, while it is likely that there is some form of executive impairment attributable to sleep loss, the specific relationship between sleep and higher cognitive functioning has been difficult to ascertain. However, one of the key factors missing from the above studies is the measurement of physiological sleep variables. It is well known that the architecture of sleep changes across the life span, in response to sleep deprivation, when sleep is placed at different phases of the circadian cycle and in response to myriad other psychological and environmental factors. To attempt to infer a particular relationship between sleep and some cognitive function based solely on the absence of a sleep period, provides no clearer picture that saying that not going to school leads to changes in cognitive function. While many studies have demonstrated that sleep deprivation exerts relatively well-understood and reliable effects on certain cognitive domains, such as sensorimotor functions and attention, the effects on executive functions remain poorly understood as studies in this area have generated conflicting results. At present, there seem to be several possible reasons for this gap in understanding.

One explanation posited by several groups (i.e. Horne and Harrison, 2000; Binks, et al, 1999) is that the majority of sleep studies have focused on simple tasks, measuring what might be deemed more basic cognitive functions (i.e. vigilance) and that there simply have not been enough investigation looking at more complex and integrated cognitive processes (i.e. executive function). Tests of vigilance generally elicit unmotivated performance on the part of the subject, due in part to their inherent monotony, and therefore they are especially sensitive to the effects of sleep deprivation and may even exacerbate otherwise subtle effects. Many studies also minimize

environmental stimulation in order to maximize the adverse effects of sleep deprivation, further exacerbating the dull nature of these tasks. Another important set of considerations relate to the limitations to formal testing of more complex cognitive processes.

Experimental sleep research often includes a period of pre-experimental training on neurocognitive tests in order to minimize the influence of practice effects by allowing performance to reach an asymptote prior to beginning the experimental period. However, many neuropsychological tests, particularly those which measure executive functions, can only be administered once before their validity is compromised by prior learning (e.x. The Wisconsin Card Sorting Test). These validity of neuropsychological tests of executive function generally hinge on their novelty, which lends further credence to the idea that the results of executive tests are influenced by a motivational component. These tests have essentially the opposite effect of more monotonous tests (i.e. tests of vigilance), in that individuals often claim to be able to rally their cognitive resources to task due to greater engagement.

The majority of neuropsychological tests were developed for clinical populations, and results are typically compared to normative samples in order to determine the degree to which an individual's performance is "neurologically normal". The typical measure for impairment in neuropsychological assessment is a relative difference from this normative sample of typically one and a half to two standard deviations. As a result, these measures may not have the level of sensitivity necessary to detect more subtle impairments in executive functioning associated with sleep deprivation, as the change may be significant within an individual, but within neurologically normal limits relative to the population. The advantages of these methods in clinical settings appear to be limitations as they are applied to experimental sleep research. Neuropsychological test

implementation poses a number of difficulties for the experimental designs which are common in sleep research (i.e. test-retest comparisons).

Finally, previous studies of executive function during sleep deprivation may have encompassed too many of the cognitive sub-components of executive function to be sensitive to the effects of sleep loss. As Goldberg and Bougakov (2005) note, it would be impossible for a single test to measure such an overarching concept as executive functioning, as the supporting networks have been found to encompass much more than the pre-frontal cortex. In other words, while fMRI and PET studies point to changes in pre-frontal function, the potential involvement of other areas of the brain creates a situation which requires an analysis of executive function that is consistent with its multifaceted nature.

Summary and Hypotheses

Increased demands on cognitive performance, like those often seen in modern work environments can place a serious burden on executive capabilities such as cognitive flexibility, divergent thinking, response initiation and inhibition, and rule attainment. These functions are often subsumed under the umbrella of "executive function". However, each specific aspect likely involves the activation of different, specific networks. Sleep, being a dynamic process of restoration and homeostatic regulation, is not uniform in its physiology or function, and various processes occurring across the different stages of sleep suggest that, to some degree, the effects that each stage has on waking function or homeostatic processes may be dissociable.

As the physiological underpinnings of sleep are increasingly well understood (Rechtschaffen and Kales, 1962; Borbely, 1982; McCarley and Hobson, 1988; Steriade, et al., 1993; Hobson et al., 2000; Hobson and Pace-Schott, 2002; Pace-Schott and Hobson, 2002), and research continues to demonstrate the negative impact of sleep deprivation on cognitive functioning (including executive functions), there is an need to clarify the relationships between sleep physiology and waking function. Significant progress has already been made with respect to some of these relationships. For instance, SWS has been shown to be important for memory consolidation, while spindle activity in stage 2 may facilitate long-term potentiation involved in memory and learning. REM sleep has been associated with the development of problem solving skills, performance on complex logic games, and the acquisition of secondary languages. REM sleep has also been linked with improved procedural learning and the elaboration and consolidation of newly acquired motor routines – often referred to as motor scripts. In addition, slow wave activity (i.e. delta frequency EEG) has been positively associated with planning, cognitive flexibility, and fluid intelligence.

Neuroimaging studies of sleep deprived individuals provides evidence that certain brain areas important for executive functioning are negatively affected by sleep deprivation. These studies have looked almost exclusively at performance on more basic cognitive tasks however, and often under conditions of total sleep deprivation. Regardless, there seems to be a growing consensus regarding diminished activation following sleep loss in the prefrontal cortex, anterior cingulate cortex, thalamus, and parietal lobes – all of which play important roles in executive function (see Thomas, et al., 2000). Studies have also demonstrated detrimental effects of sleep loss in the superior parietal lobule and parietal operculum, whose functions may support the behavioral output of executive functions.

Furthermore, cognitive decrements following from both partial and total sleep deprivation include diminished memory functioning, impaired learning, problems with creative/divergent thinking, cognitive flexibility, and supervisory control (Horne, 1988; Wimmer et al., 1992; Nilsson et al., 2005), though some research does not support these latter findings (i.e. Binks, et al. 1999). Generally, prior research suggests that while sleep loss is associated with decreased activity in areas of the brain which are important for executive function, the relationship between these two is complex. Mapping this relationship requires an appreciation for the dynamic nature of sleep and the multifaceted nature of executive function.

To this end, few studies have investigated the role of different sleep stages on the components of executive function, looking instead at the impact of total sleep deprivation on subsequent waking performance. While it is relatively well established that deficits in executive function follow from extended periods of total sleep loss, the aspects of sleep that are important for executive functioning are largely unclear since all stages of sleep are lost completely in these studies.

Hobson and Pace-Schott (2002) suggest that, with regard to memory consolidation, SWS is related to the reiteration of information, while REM sleep is involved in integrating this information with prior knowledge. Based on this model, it follows that executive capacities are differentially related to REM sleep and NREM sleep. It seems, based upon Anderson and Horne's (2003) findings, that slow wave activity is positively associated with certain aspects supporting executive performance such as those mentioned throughout this paper, while REM may be associated with the acquisition of problem solving skills and new cognitive and motor routines (Smith, 1996). The purpose of this study is to investigate the relationship between the aforementioned executive functions and sleep physiology. Specifically, this study will address the following questions:

(1) What are the relationships between electrophysiological sleep variables and executive performance?

(2) How is executive functioning affected by chronic partial sleep restriction?

The "Sleep in America Survey" (National Sleep Foundation, 2002) findings suggest that individuals do not typically lose entire sleep periods, but restrict their sleep periods chronically (see Introduction), often getting less than necessary to allow for optimal waking function. This study differs from many prior investigations of sleep and executive functioning in that, individuals had their sleep restricted rather than eliminated altogether, offering greater ecological validity.

This study also differs from previous research in that the relationship between sleep physiology, rather than presence or lack of sleep, was examined for potential predictive value of each stage for executive performance. Furthermore, executive functioning was broken into subcomponents: divergent thinking, cognitive flexibility, response initiation and inhibition, and rule attainment. These were derived from the Hayling Sentence Completion Test and Brixton Spatial Anticipation Test (Burgess & Shallice, 1997).

While the Hayling and Brixton tests have not been frequently used in the sleep or neuropsychological studies, they have been shown to have adequate internal and external validity (Odhuba, et al., 2005) for clinical populations and provided an opportunity to corroborate and complement research which has used other executive tests, such as the Wisconsin Card Sorting Test, Trails Test versions A and B, the Stroop Color/Word Test, and others. The Hayling Sentence Completion Test was used to assess divergent thinking, response initiation, and response inhibition. The Brixton Spatial Apperception Test was administered to assess rule attainment and cognitive flexibility. In addition, since this was part of a larger study investigating the effects of chronic partial sleep restriction, other tests were administered throughout the protocol, assessing sustained attention and working memory, which have been previously demonstrated be sensitive to sleep restriction. These latter measures were examined to determine whether the experimental manipulation (i.e. sleep restriction) produced effects on cognition similar to what has previously been reported (e.g. Horne, 1985, 1988; Van Dongen, 2003).

Based on evidence from previous studies, slow wave sleep appears to be the portion of sleep most frequently associated with executive functions and the restoration of frontal brain areas. The following hypothesized relationships were evaluated in this study:

1. Slow wave sleep was hypothesized to be the best predictor of overall executive function (a sum of the component measures).
2. It followed from the previous prediction and existing research that the specific elements of executive function, as they are conceptualized in this study to include response initiation, response inhibition, cognitive flexibility, divergent thinking, and rule attainment should be related to the

amount of SWS obtained in the prior sleep period as well, though perhaps not all subcomponents would be affected similarly by sleep restriction.

As slow wave sleep has often been associated with performance on tasks of sustained attention and working memory,

1. SWS was predicted in this study to be related to:
    a. Sustained attention and;
    b. Working memory.

Next, as several studies have illustrated the importance of REM sleep in the learning of new cognitive (though mostly motor) routines and logical problem solving, it seemed that REM might be expected to serve a role in cognitive flexibility and divergent thinking, since these skills are often an essential part of problem solving and tend to require the ability to learn from one's experience. Thus, while to a lesser degree than SWS:

2. The total amount of REM sleep (minutes) was also hypothesized to predict:
    a. Overall executive function.
    b. Cognitive flexibility.
    c. Divergent thinking.

A secondary question which we attempted to address with this study was whether chronic partial sleep restriction led to decrements in overall executive function relative to normal sleep (i.e. 8h/night) over the same time period (5 consecutive nights). Based on a large body of research reviewed earlier, it was hypothesized that sleep restricted individuals would demonstrate some degree of executive dysfunction, though the specific aspects of executive function affected could not be determined a priori.

3. Thus, relative to 5 consecutive nights of normal sleep, sleep restricted individuals were predicted to demonstrate:

a. Decrements in divergent thinking,
b. Decrements in cognitive flexibility,
c. Decrements in response initiation,
d. Decrements in response inhibition.
e. Decrements in rule attainment.

As mentioned, sustained attention and working memory have been previously demonstrated as highly sensitive to the effects of sleep loss.

4. Therefore, given that these relationships have been demonstrated in the past, we hypothesized that chronic partial sleep restriction would be associated with:
    a. Decrements in sustained attention and;
    b. Decrements in working memory.

Methods

Participants

N = 137 (n = 120 sleep restricted participants; n = 17 control participants) adult participants aged twenty-two to forty five years, with sixty females and seventy-seven males of various ethnicities completed the protocol with adequate data for analysis. Individuals were recruited via newspaper, radio, and internet advertisements. Potential participants were first screened extensively by telephone. Following this initial screening and prior to beginning the protocol, an in-laboratory screening session was conducted. During the first in-laboratory screening session, the study was described to each potential participant, informed consent was obtained, and a complete and confidential medical screen. In addition, a series of questionnaires regarding sleep-wake patterns and experiences with sleep deprivation was administered. In order to ensure a comprehensive screening of sleep-wake patterns, potential participants completed sleep diaries and wore wrist actigraphs (Actiwatch, MiniMitter Inc., OR) for 7 consecutive days prior to attending a second in-laboratory screening session. During the second screening session, actigraphic data were compared to the sleep log, and if participants met the sleep inclusion criteria described above, they returned to the laboratory for a third screening session to tour the research facility and undergo a full physical exam, including blood and urine assays at the General Clinical Research Center (GCRC) of the Hospital of the University of Pennsylvania. Qualified participants were then given the opportunity to practice the computerized neurobehavioral testing. However, the neuropsychological tests of executive function were not administered, as this would invalidate subsequent test results.

Physical health was established based on a self-report of clinical history, as well

as blood and urine tests and a physical examination carried out prior to the experiment. Any participants with symptoms of active physical or mental illness were excluded from the study. Participants were determined to be comparable in terms of their homeostatic and circadian sleep-wake regulation parameters (criteria 1, 3, 4, 5 below). In order to participate in the study, participants had to meet the following inclusion criteria:

1. Age 22 to 45 years
2. Body mass index within 15% of normal
3. No shift work, trans-meridian travel or irregular sleep/wake routine in past 60 days
4. Stable, normally-timed sleep-wake cycle as determined by interview, 2-week daily sleep log, and 2-week wrist actigraphy. Including
    a. Habitual nocturnal sleep duration between 6.5h and 8.5h.
    b. Habitual morning awakening between 0600h and 0900h.
    c. No evidence of habitual napping.
5. No sleep disorder, as determined by history, actigraphy, or baseline polysomnography.
6. No current depression as measured by the Beck Depression Inventory
7. No alcohol or drug abuse in the past year based upon history and urine toxicology screen
8. Not a current smoker
9. No acute or chronic, debilitating medical conditions.
10. No major Axis I psychiatric illness, epilepsy, or thyroid disease, based on history, physical exam, blood and urine chemistries, and CBC.

Procedures

Qualified participants were invited to enroll in the study. Throughout the protocol, participants resided in the Sleep and Chronobiology Laboratory (SCL) facility at the

Hospital of the University of Pennsylvania. After two baseline nights of sleep, participants underwent a period of chronic sleep restriction of 4h time in bed for sleep per night for 6 consecutive nights. Strict environmental controls and a constant routine were employed to minimize experimentally unrelated sources of variance. Light conditions were less than 50 lux waking periods and less than 1 lux during sleep periods to control for potential circadian variability. Participants were also monitored 24h/day by trained staff to ensure adherence to the protocol. Nutritionally balanced meals were provided at regular meal times throughout the protocol, and caffeine, nicotine, and alcohol were prohibited during the experiment. Throughout the experimental protocol, computerized neurobehavioral test batteries were administered at regular intervals, including a wide range of tasks (described below). On the final day of sleep restriction, following 5 nights of restricted sleep, the Hayling Sentence Completion Test and the Brixton Spatial Apperception Test (described below) were administered by trained staff during the late morning. The timing of administration for these tests was not consistent between participants.

Measures

Sleep

Sleep periods were recorded by polysomnograph (PSG) (Suzanne Ambulatory PSG, Mallinckrodt) on both baseline days and on 3 of 5 sleep-restriction days. Participants were monitored continuously through infrared cameras throughout all sleep periods, which will provide an additional means by which to verify TIB. All PSG recordings were obtained from standard electrode locations (C3-A1A2, O1-A1A2, LOC-ROC, EMG determined using the standard 10-20 system). PSG data were downloaded to computers and processed via traditional sleep stage scoring criteria (Rechschaffen and Kales, 1960). Latency to each sleep stage, sleep duration, sleep efficiency, wake

after sleep onset, and absolute and proportional amounts of each stage of sleep were determined. For the present study, these variables will be derived from the sleep period occurring just prior to the administration of the Hayling and Brixton tests.

Executive Functioning: The Hayling and Brixton Tests

Performance on the Hayling Sentence Completion Test and Brixton Spatial Anticipation Test (Burgess and Shallice, 1997) were assessed following sleep restriction. The Hayling and Brixton tests were standardized on anterior and posterior unilaterally lesioned patients, bilateral frontal lesioned patients, and healthy controls. In the standardization sample, no laterality effects were found on any measure from the Hayling test. Controls performed significantly better than frontal lesioned patients, but anterior/posterior comparisons did not reach significance, suggesting that this test is sensitive specifically to frontal lobe deficits. The authors urge caution when interpreting Hayling test results for individuals who fall within the bottom 15% of the population on measures of general intelligence in light of Burgess' (1997) findings that suggest there is more variability in these individuals' scores. To account for this in the analysis, The North American Adult Reading Test (NAART) was administered to provide an estimate of general intelligence quotient.[2]

The Hayling Sentence Completion Test

The Hayling Sentence Completion Test consists of two parts administered in succession. Each part includes the same set of fifteen sentences with the last word omitted. In part 1 each sentence is read aloud by the experimenter (i.e. The captain wanted to stay with the sinking…") and the participant must verbalize a response which fits sensibly within the context of the sentence (i.e. "ship"). In Part 2, the same set of

[2] Any participant with an IQ (as estimated by the NAART) at or below the 15th percentile was excluded from the data analysis to avoid potential confounding effects of intelligence on executive function outcomes.

fifteen sentences are again read aloud by the experimenter (i.e. The captain wanted to stay with the sinking…"), but the participant is asked to verbalize a response which does not fit sensibly within the context of the sentence is given verbally by the participant (i.e. "light bulb"). Both parts provide a measure of: (1) basic task initiation speed, which is the sum of the response latencies. This measure has been shown to be impaired in individuals with frontal lobe lesions (Burgess & Shallice, 1997). Part 2 yields a measures (2) Response suppression based on the number of errors, and two categories of errors: (3) Category A errors, which are those which are either repetitions of a previous response (after the participant has been instructed not to do so) or a response which completes the sentence sensibly and (4) Category B errors, which are those in which the participant completes the sentence with a word which is related to the context of the sentence and/or is somewhat plausible. Another measure which is derived from part 2 is (5) Efficiency, or the time it takes for the individual to produce a correct response. Determining the style of failure on Part 2 is important and can be done by comparing error scores and response times. Impulsive individuals tend to respond quickly, but make frequent errors, while people who have difficulty disengaging from the expected response may make the opposite trade-off. This task was completed once during the protocol, and trained scorers carried out double blind scoring of performance. In the standardization sample, Burgess and Shallice (1997) note that the mean (SD) scaled scores for errors on Hayling parts 1 and 2 was 6.4 (1.7) for controls, 4.4 (2.3) for individuals with unilateral anterior lesions, 2.2 (2.0) for bifrontally lesioned individuals, and 6.3 (1.5) for individuals with unilateral posterior lesions.

The Brixton Spatial Anticipation Test

The Brixton Spatial Anticipation Test measures rule attainment, rule following, and cognitive flexibility. Participants are presented with fifty-six pages of an array of ten

circles, one of which is filled in with red ink. Participants must determine where the red circle will appear next in the array without any feedback on their performance. Impairments on the Brixton have been frequently associated with dysexecutive problems, in that Individuals with frontal lesions tended to make more guessing errors than those with posterior lesions or controls and bifrontally lesioned patients performed more poorly than the unilaterally frontal lesioned patients (though not statistically significant), or controls (significant) (Burgess & Shallice, 1997). Two measures are derived from the Brixton - total errors (a measure of rule attainment) and perseverative errors (a measure of cognitive flexibility). Rule attainment, as measured by the Brixton Test, was significantly correlated with self-report measures of dysexecutive symptoms in a recent study of frontally lesioned patients (Odhuba, et al., 2005). The Brixton Spatial Anticipation Test was also completed once during the protocol, and trained scorers carried out double blind scoring of performance on this task as well. In the standardization sample, Burgess and Shallice (1997) reported that the mean (SD) number of errors on the Brixton Test was 16.0 (5.7) for controls, 24.5 (9.0) for individuals with unilateral anterior lesions, 30.7 (12.0) for bifrontally lesioned individuals, and 18.3 (7.2) for individuals with unilateral posterior lesions.

Attention/Vigilance: The Psychomotor Vigilance Task (PVT)

The PVT is a simple reaction time test in which individuals watch a computer screen until a counter appears in the center of a box in the middle of the screen. Participants are instructed to press a button on a two button response box (left handed individual press the left button and right handed individuals press the right button) as soon as the stimulus appears. The test is designed to evaluate sustained attention and, for the purposes of this study, total number of lapses (response times >500ms) will be assessed.

Working Memory: The Working Memory Task

The working memory task (WMT) is an n-back task, which requires subjects to determine whether a letter presented on the monitor (target stimulus) is the same or different from a letter previously displayed on the monitor (cue stimulus). This task requires subjects to maintain information and update this information in working memory. Difficulty on this task is manipulated by changing the interval between the cue stimulus and target stimulus. The primary outcome of interest for this task will be the percentage correct responses.

Statistical Approach

A stepwise linear regression procedure was conducted to assess the presence and degree of association between the executive function variables derived from the Haylings and Brixton Tests and three electrophysiological sleep variables: stage 2 sleep, SWS, and REM sleep. Sustained attention and working memory, evaluated using the Psychomotor Vigilance Task and Working Memory Task (n-back) respectively, were also analyzed using stepwise linear regression in order to specify the relationships of these more basic cognitive functions to the aforementioned sleep variables.

Our secondary analysis involved comparisons of the performances of sleep restricted and control participants using student's t-tests for between group differences on all measures of executive functioning as well as measures of sustained attention and working memory.

Dependent Variables:

Executive Function:

1. Overall executive function: Composite score - Sum of Hayling and Brixton scaled scores.
2. Divergent Thinking: Category B errors on part B of the Hayling Sentence Completion Test.

3. Cognitive Flexibility: Total number of errors on the Brixton Spatial Anticipation Test.
4. Response Initiation: Total latency on part B of the Hayling sentence completion test.
5. Response Inhibition: Category A errors + Category B errors on the Hayling Sentence Completion Test.
6. Rule Attainment: Overall Brixton Spatial Anticipation Test scaled score.

Other Cognitive Functions:

7. Sustained Attention: PVT lapses
8. Working Memory: WMT total percent correct

Independent Variables:

Sleep Physiology

A. Total sleep duration in minutes from lights out to lights on (TST)
B. Absolute minutes of stages 2
C. Absolute minutes of SWS (stages 3 & 4 combined)
D. Absolute minutes of REM sleep

Results

This study assessed the relationship between electrophysiological sleep variables, obtained following five nights of sleep restricted to four hours, with measures of executive function assessed using the Haylings and Brixton tests. A total of n = 120 sleep restricted participants completed the study, sleeping an average of 3.88 hours per night (*SD* = 0.25 hours). For comparison, a control group of n = 17 control participants, who slept an average of 7.95 hours per night (*SD* = 0.97 hours), were included for a secondary analysis as described below. Demographic variables are summarized in Table 1.

The average total sleep time in minutes, as well as the average total minutes of Stage 2 sleep, REM sleep, and SWS for both sleep restricted participants and controls are summarized in Table 2. T-tests for the differences demonstrated significantly greater amounts of stage 2 sleep ($p < .05$) and REM sleep ($p < .05$), but preservation of total minutes of SWS ($p > .05$) in the control group versus the sleep restricted group.

Performances of both groups on the Haylings Sentence Completion Test and Brixton Spatial Anticipation Test were within the average range relative to the normative sample on all dependent measures (Burgess & Shallice, 1997). Means and standard deviations for the dependent measures are summarized in Table 3. Scaled scores above 5 (>25th percentile) for the Hayling and Brixton tests were considered Average (Burgess & Shallice).

Additionally, to ensure valid testing, the North American Adult Reading Test (NAART) was administered prior to the experimental manipulation to ensure that all subjects had an adequate baseline reading level prior to testing. All participants (sleep restricted and control) obtained scores within testable limits on the NAART.

A stepwise linear regression procedure was conducted to assess the presence and degree of association between the executive function variables derived from the

Haylings and Brixton Tests and three electrophysiological sleep variables: Stage 2 sleep, SWS, and REM sleep. Sustained attention and working memory, evaluated using the Psychomotor Vigilance Task and Working Memory Task (n-back) respectively, were also analyzed using stepwise linear regression in order to specify the relationships of these more basic cognitive functions to the aforementioned sleep variables. All dependent measures of executive function were correlated ($p < .01$). Cognitive flexibility and response initiation were also correlated with age ($p \leq .05$). Despite this, these measures were analyzed independently to investigate whether they each was significantly related to the physiological sleep variables. Slow wave sleep was correlated with age ($p < .05$), but not sex. Some of the independent measures were correlated as well, though none of the correlation coefficients exceeded a magnitude of $r = .50$, suggesting no violation of the assumption of collinearity. Total sleep time was correlated with SWS ($p < .05$). However, since the primary hypothesis regards relationships involving sleep physiology (i.e. specific sleep stages), total sleep time was not included as an independent measure in the final analysis. See Table 3 for a summary of significant correlations. In a preliminary analysis using a stepwise regression including all sleep measures, total sleep time was not found to be a significant predictor of performance on any of the executive function measures.

Our secondary analysis (referred to above) involved comparisons of the performances of sleep restricted and control participants using T-tests for between groups differences on all measures of executive functioning as well as measures of sustained attention and working memory.

Relationships between electrophysiological sleep variables and executive functions

The primary hypothesis for this study was that SWS would be the best predictor of overall executive functioning. As noted, an individual's overall executive function was operationalized as the sum of his or her scaled scores on the Haylings and Brixton tests.

Figure 1 illustrates that our hypothesis was supported, and overall executive function was significantly and positively associated with minutes of SWS occurring on the night prior to testing and following five nights of sleep restriction to four hours in bed for sleep (beta = 0.290, $p < .001$). These results suggest that SWS likely supports the performance of frontal and executive functions. However, each additional minute of total SWS was associated with only a marginal increase in the overall score. While influential on performance, SWS accounted for only 8.4% (R^2 = .084) of the variance in overall executive function, suggesting its role in the performance of these tasks is limited. Observed power, by post hoc analysis was 0.71.

While our primary hypothesis was supported, we also predicted that the cognitive subcomponents of executive function measured in this study, including response initiation (response latency on part 2 of the Hayling Sentence Completion Test), response inhibition (total number of errors "Category A & B" on parts 2 of the Hayling Sentence Completion Test), cognitive flexibility (total number of errors on The Brixton Spatial Anticipation Test), divergent thinking (number of "Category B" errors on part 2 of the Hayling Sentence Completion Test), and rule attainment (scaled score on the Brixton Spatial Anticipation Test) would also be significantly related to total minutes of SWS.

As hypothesized, SWS was the best predictor of response initiation out of the three sleep variables included in the analysis. Specifically, response initiation was significantly, negatively associated with total minutes of SWS on night 5 (b = -0.260, p = .004), such that additional minutes of SWS were associated with shorter response latencies on part 2 of the Hayling Test (see Figure 2). However, similar to the results for overall executive functioning, the proportion of variance in response latencies explained by total minutes of SWS was less than 10% (R^2 = .068). Other stages of sleep (i.e. REM sleep, Stage 2 sleep), were not significantly related to speed of responses on the part 2 of the Hayling test.

Next, we hypothesized that SWS would predict response inhibition. This hypothesis was also supported, and response inhibition was significantly associated only with SWS (beta = -0.209, *p* = .020), such that participants with a greater total number of minutes of SWS on night 5 of sleep restriction made fewer errors of the kind that were sensible completions of the sentence or which were repetitions of previous responses (Figure 3). The proportion of the original variance in response inhibition accounted for by the minutes of SWS was very small, at 4.3% (R^2 = 0.043).

Divergent thinking was operationalized as the number of sensible completions of sentences when non-sensible responses were called for. SWS was hypothesized to be the best predictor of this measure, and results supported this hypothesis. Figure 4 illustrates that total number of "type b" errors was negatively associated with minutes of SWS (beta = -0.197, *p* = .031), though again only accounting for 3.9% of the variance (R^2 = 0.039). In other words, additional minutes of SWS predicted fewer errors which were sensible completions of the sentence, when a non-sensible response was required.

We also hypothesized that cognitive flexibility would be associated with the total minutes of SWS on night five of sleep restriction. Total minutes of SWS on night 5 was the best predictor of cognitive flexibility, with more minutes of SWS predicting fewer errors on the Brixton test (beta = -0.231, *p* = .011). Once again however, the amount of variance in this dependent measure that was accounted for by minutes of SWS, was small at 5.3% (R^2 = 0.053).

The final component of executive function assessed in this study was rule attainment, which reflected participants' ability to ascertain rules from an ambiguous situation and alter their strategies based on the feedback (correct, incorrect) that was provided to them by the experimenter. Of the three sleep variables analyzed, SWS was the only significant predictor of this measure (beta = 0.201, *p*= .030). A greater amounts

of SWS on night five was associated with better overall performance on the Brixton test, again with less than 5% of the variance accounted for by SWS (R^2 = 0.032).

We hypothesized that REM would also be significantly related to overall executive performance, and specifically to the subcomponents: divergent thinking and cognitive flexibility. However, results did not support these hypotheses (all p >0.05). Further, as expected, no significant associations were demonstrated between total minutes of Stage 2 sleep and any of the dependent executive function measures (all p > 0.05).

Finally, the correlation between age and SWS suggested that the observed relationship between SWS and the dependent executive function measures may be better explained by the effect of age on the performance of the Hayling and Brixton tests. When included as an independent variable in the regression analyses, age was not found to be a significant predictor of any of the dependent measures. This suggests that SWS is uniquely related to executive function.

How is executive functioning affected by chronic partial sleep restriction?

The secondary analysis, see above, was used to determine whether five nights of sleep restriction to four hours time in bed for sleep each night would be associated with decrements in executive functioning, with consequent decrements in divergent thinking, cognitive flexibility, response initiation, response inhibition, and rule attainment. Previous studies have demonstrated detrimental effects of chronic partial sleep restriction on cognitive functions including sustained attention and working memory. We therefore hypothesized that sustained attention (total PVT lapses) and working memory (percent correct on the WMT) performance would also be significantly different between the two groups. These hypotheses were assessed using T tests (SPSS, 15.0.0, SPSS Inc., Chicago, IL, 2006) for significant differences between a group of sleep restricted participants (n = 120) and controls (n = 17).

Significant differences were demonstrated on several, but not all variables (results are summarized in Table 4). Sleep restricted participants demonstrated significantly longer response latencies relative to controls on the Hayling test ($t(36.35) = -3.106$, $p = .004$, $M_{(controls)} = 15.94$; $M_{(sleep\ restricted)} = 26.95$). In addition, a significant difference was found for a related measure of efficiency, which was measured as the amount of time in seconds to produce a correct response on The Hayling Sentence Completion Test, part B ($t(40.81) = -2.600$, $p = .013$; $M_{(controls)} = 1.70$; $M_{(sleep\ restricted)} = 3.42$). There was also a non-significant trend for fewer b-type errors on part B of the Hayling test in the control group relative to sleep restricted participants ($t(25.18) = 1.97$, $p = .084$; $M_{(controls)} = 1.59$; $M_{(sleep\ restricted)} = 2.50$), a measure reflecting divergent thinking.

Results indicated there were significant differences, as predicted, between sleep restricted participants and controls on a test of sustained attention (attentional lapses on the PVT) administered in the morning following the fifth night of sleep restriction within one hour of the HBT ($t(96.50) = 6.943$, $p < .001$). Sleep restricted individuals had a greater number of lapses, and increased variability compared with those sleeping 8h per night for 5 consecutive nights ($M_{(sleep\ restricted)} = 10.16$, $SD_{(sleep\ restricted)} = 10.74$ vs. $M_{(control)} = 1.75$, $SD_{(control)} = 2.64$). Contrary to our hypothesis that sleep restriction would be associated with decrements in working memory performance relative to controls, results demonstrated no significant difference between sleep restricted participants and controls on percent of correct responses on the Working Memory Task ($p > .05$).

Consistent with our primary hypotheses, the results of these analyses demonstrated significant relationships between SWS and overall executive function and executive subcomponents. Furthermore, compared with controls sleeping eight hours per night for five consecutive nights, sleep restricted participants demonstrated significantly longer response latencies and took longer to produce accurate responses on part B of the Hayling Sentence Completion Test, reflecting diminished capacity for response initiation

and efficiency. A significant trend for fewer type B errors on part B of the Hayling test suggests greater amounts of SWS are predictive of increased capacity for divergent thinking. However, contrary to our hypothesis that working memory performance would be negatively impacted by sleep restriction, no significant difference was found.

Discussion

The results of this study, with respect to our primary hypothesis, are in line with similar studies in this area (Horne, 1988; Wimmer et al., 1992; Anderson & Horne, 2003; Gosselin, et al., 2005; Nilsson et al., 2005). Slow wave sleep was the best predictor of overall executive function, and each executive subcomponent as they were conceptualized in this study. The degree of association, while significant, never accounted for greater than 10% of the variance in any executive measure however. This suggests that while there is likely some role for slow wave sleep in supporting executive function, this role is but a small piece of the picture and may be negligible for performing tasks involving rule attainment, cognitive set shifting, flexibility, initiation and inhibition.

Despite the small effect size, these findings support the hypothesis that individuals with greater amounts of SWS perform significantly better on tasks involving divergent thinking, rapid response initiation, and inhibition of inappropriate responses, cognitive flexibility, and the ascertainment of rules from ambiguous situations. Furthermore, executive function benefits from greater amounts of SWS to the exclusion of other physiological sleep states such as REM or stage 2 sleep.

As expected, based on the existing knowledge of the neural substrates of executive function and how they are differentially effected by sleep loss, sleep restricted individuals performed worse on some measures of executive function, but not others. While response initiation, behavioral (verbal) inhibition and divergent thinking were shown to be susceptible to chronic partial sleep restriction, rule attainment and cognitive flexibility were not significantly worse in sleep restricted participants when compared to the performance on controls sleeping a full 8h per night.

As a test of whether our intervention (i.e. chronic partial sleep restriction to 4h per night for 5 consecutive nights) replicated the effects of similar studies, comparisons between groups revealed that sleep restricted participants demonstrated expected

decrements in performance. As reported in previous studies (Dinges, 1985, Dinges & Kribbs, 1991, Durmer & Dinges, 2005, Van Dongen), sleep restricted individuals demonstrated significantly poorer performances on a sustained attention task. Conversely, results of the working memory task did not exhibit the expected differences between sleep restricted participants and controls, though again, it is likely the number of control subjects (n = 17) may not have been sufficient to capture this effect or that our measure of working memory was not sufficiently sensitive.

Cognitive flexibility, creative thinking, response initiation and inhibition, and rule attainment comprise a critical set of abilities which allow us to manage complexity, solve problems, and perform optimally in everyday work environments. With multi-tasking an essential skill for many modern professions, the need for their reliable function cannot be understated. It is widely agreed that these higher-order abilities, often subsumed under the umbrella of executive function, are associated with frontal lobe functions. However, executive functions are currently being associated with activity in a variety of other brain areas as well, including the thalamus, the anterior cingulate cortex and areas of the parietal cortex. Importantly, previous research has demonstrated changes in activation in these areas following sleep loss (Thomas et al., 2000; Drummond et al., 2005).

Despite extensive scientific evidence supporting the claim that a lack of adequate sleep leads to increased risk for health problems, reduced productivity, and compromised safety, sleep deprivation has been, and continues to be, linked to numerous accidents and catastrophic failures in real-world situations (Herscovitch, et al., 1980; Johnson, 1982; Mitler, et al, 1988; Dinges and Kribbs, 1991; D'Alessandro, et al, 1995; Dement, 1994; Belenky, et al, 1994; Baldwin and Daugherty, 2004; Lockley, et al., 2004; Van Dongen, et al, 2004; Durmer and Dinges, 2005). However, despite these findings and the evidence from neuroimaging studies, there remains some uncertainty as to whether executive functioning is similarly susceptible to sleep loss (see

Herscovitch, 1980; Binks, et al., 1999). It is thus important to clarify the relationship between sleep and executive function as there are clearly many individuals who fail to obtain adequate sleep and for whom the ability to multi-task, maintain appropriate behavior, and deal effectively with novel situations are essential to their performance.

There has been difficulty in clarifying the relationships between sleep stages and cognitive functions which a rooted mainly in the traditional approach to conducting sleep research. The relationships between sleep and cognitive functions have frequently been inferred by identifying brain areas impacted by sleep loss (i.e. via EEG or fMRI) or by measuring performance on cognitive tests after periods of total sleep deprivation or restricted sleep. However, few studies exist which establish well defined relationships between sleep stages and specific cognitive abilities such as executive function. Those studies which have looked at these relationships have generally focused on relatively basic cognitive functions such as attention or processing speed. However, despite the currently limited research in this area, mounting evidence suggests that sleep loss has an impact on executive function and that SWS in particular may be important for the restoration of certain executive functions (Anderson & Horne, 2003). The results of the present study suggest that these issues warrant further study.

An additional goal was to determine whether chronic partial sleep restriction exerts similar effects on executive function as total sleep deprivation, by comparing the performances of sleep restricted participants with that of controls and determining whether any differences were congruent with similar findings in other studies. Based on results of this study, it appears that SWS supports executive function as well, at least with respect to response initiation, inhibition, and possibly rule attainment. However, further studies are necessary to clarify the nature of the effects of chronic partial sleep restriction on other executive functions. Slow wave sleep appears to serve a restorative function for those brain areas involved in each of the various executive functions.

Limitations and Future Directions

Physiological sleep variables accounted for, at best, minimal variance in executive function in this sample. Despite reaching statistically significant levels on measures of association, the amount of variance in all factors explained by sleep variables was never more than 10% and often much lower, suggesting that other factors affecting test performance on the Hayling, Brixton, PVT, and WMT, beyond sleep variables, were missing from the regression model. Also, chronic partial sleep restriction to 4h per night for 5 consecutive nights did not significantly affect certain functions considered to be executive in nature such as rule attainment, cognitive flexibility, or response inhibition relative to controls sleeping 8h per night.

The small effect size and failure to demonstrate differences between sleep restricted participants and controls may have several explanations. One alternative is that the sensitivities of the Hayling and Brixton tests were not sufficient to capture the full effect SWS has on subsequent executive function. This potential limitation to the current study may be addressed in future studies either by employing a more comprehensive approach to assessing executive function, such as a battery of tests like the Delis-Kaplan Executive Function Scale. Another possible explanation is that, while chronic partial sleep restriction exerts similar effects to total sleep deprivation on sustained attention, the same is not true of more complex, integrative functions. Possibly, executive functions are more resilient to chronic partial sleep restriction due to the more distributed nature of brain activity involved with their performance. More sensitive tests may simply measure more basic abilities which rely on more limited brain areas (i.e. sustained attention and the thalamus).

Neuropsychological test batteries allow for the decomposition of performance into relatively orthogonal categories, such as sensory and perceptual functions, attention, concentration, verbal and perceptually mediated learning, memory, and processing

speed, as well as speech, language, and executive functions. This is accomplished by the administration of large number of tests which, more or less, target those specific cognitive domains and allow for clinicians to partial out the differential effects of brain dysfunction on these and other cognitive domains. While this approach offers clinicians the benefit of disentangling the overlap in the types of abilities involved in a given task by comparing performance across testing, it is often too cumbersome for research protocols as it is time and effort intensive and involves a considerable amount of clinical interpretation. As a result, there appears to be a need for the development of a more comprehensive and repeatable battery for assessing executive function to address this limitation.

It is important to note that while tests of executive function and attention are routinely part of clinical neuropsychological assessments, sleep history does not typically factor into clinical interpretations and may not even be addressed when obtaining the patient's history. In fact, given solely the well established effects of sleep loss on attention, there is an alarming absence of studies investigating the impact of sleep loss on other domains of clinical neuropsychological testing, such as memory, language, processing speed, and of course, executive function. The possibility of sleep loss acting as a confound when interpreting neuropsychological data is real. However, a search of PubMed for "sleep and clinical neuropsychology" yields only two papers which have little to do with the relationship between sleep and neuropsychological testing. Based on the findings of ours and others' studies, it seems likely that sleep loss is a more important factor in waking cognitive function than most clinicians currently appreciate and sleep seems to be, as of yet, an underestimated factor for interpreting neuropsychological test results.

For patients with issues ranging from an undiagnosed sleep disorder, to reduced sleep on the night prior to neuropsychological testing due to anxiety, to chronically

reduced sleep time due to a heavy work schedule, it is at present unclear to what degree measures of their neuropsychological functioning are being impacted by sleep loss. Investigations looking at changes in executive function following sleep loss have produced varied results, with some findings significant decrements (i.e., Horne, 1988, Harrison & Horne, 2000, Gosselin et al., 2005, Nilsson et al., 2005) and others demonstrating no specific deficit in executive abilities (i.e. Wimmer et al. 1992, Binks et al., 1999, and more recently Verstraeten, et al., 2004). This study appears to support some role, albeit small, for SWS in the performance of certain executive tasks.

Finally, irrespective of the effects of sleep loss on executive function, it is clear that sleep variables, such as total amount of sleep and amount of particular stages of sleep, have important and as of yet incompletely defined relationships with cognitive function. As such, it is clear that more basic research is needed in determining the specific relationships between sleep physiology and waking neuropsychological functions. Research in this area can and should be used to inform clinical interpretations. More generally, these types of studies are necessary bring public awareness to the impact of sleep loss on waking cognitive performance.

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Table 1

Summary Statistics for Demographic and IQ Variables

		Min	*Max*	*M*	*SD*
Control					
	Age	23.00	44.00	29.82	6.88
	NAART - full IQ	94.26	118.44	107.29	7.57
	NAART - verbal IQ	90.43	118.02	105.30	8.64
	NAART - performance IQ	101.34	114.36	108.36	4.08
Sleep Restricted					
	Age	22.00	45.00	29.98	6.64
	NAART - full IQ	83.34	123.12	106.12	8.36
	NAART - verbal IQ	77.97	123.36	103.96	9.54
	NAART - performance IQ	95.46	116.88	107.72	4.50

Table 2
Means and Standard Deviations of Sleep Variables

Group	*Sleep Measure*	*M*	*SD*
Sleep Restricted			
	Total sleep time	232.74	15.35
	Stage 2 Sleep	102.97	31.07
	SWS (Stages 3 and 4)	62.49*	31.66
	REM sleep	57.64	15.12
Control			
	Total sleep time	477.18	58.36
	Stage 2 Sleep	263.85	35.63
	SWS (Stages 3 and 4)	54.68*	40.80
	REM sleep	106.26	27.50

Note. Sleep Restricted participants (n=120) had four hours time in bed for sleep for five consecutive nights. Control participants (n=17) had ten hours time in bed for sleep for five consecutive nights. Means and standard deviations are presented in minutes. All sleep variables were significantly different between groups with the exception of SWS. *($p > .05$).

Table 3
Pearson Correlations: Age, Sleep, and Executive Function Variables

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Age	--	*-0.22**	0.14	*-0.34***	0.13	*0.18**	0.09	0.17	-0.16	-0.12	-0.20*	-0.21*	0.10
2. Total Sleep Time		--	0.02	0.30**	0.10	-0.13	-0.21*	-0.13	0.10	0.21*	0.06	0.01	-0.26**
3. Stage 2			--	-0.43*	-0.36**	0.23*	0.11	0.13	-0.11	-0.20*	-0.06	-0.09	0.10
4. SWS				--	-0.06	*-0.26***	*-0.20**	*-0.24***	*0.21**	*0.30***	0.10	*0.24***	*-0.21**
5. REM Sleep					--	-0.10	-0.09	0.02	0.00	0.12	0.13	-0.09	-0.10
6. Response Initiation[a]						--	0.58**	0.26**	-0.25**	-0.67**	0.21*	-0.11	*0.56***
7. Divergent Thinking[b]							--	0.26**	-0.26**	-0.75**	0.01	-0.16	*0.93***
8. Cognitive Flexibility[c]								--	-0.96**	-0.65**	-0.03	-0.11	*0.31***
9. Rule Attainment[d]									--	0.66**	0.03	0.04	*-0.31***
10. Overall Executive Function[e]										--	-0.07	0.15	*-0.82***
11. Sustained Attention[f]											--	-0.08	0.00
12. Working Memory[g]												--	*-0.23**
13. Response Inhibition[h]													--

Note. Pearson correlations (*r)* are shown above with significant correlations flagged. All sleep stage variables were measured in minutes.
[a] Hayling part B latency; [b] Hayling category 'B' errors; [c] Brixton errors; [d] Brixton scaled score; [e] Hayling and Brixton sum of scaled scores; [f] PVT lapses; [g] N-back percent correct; [h] Hayling sum of 'A' and 'B' errors.
*$p < .05$
** $p < .01$

Table 4
Means and Standard Deviations for all Hayling and Brixton Measures

Hayling/Brixton Measure	*Condition*	*M*	*SD*
Overall Executive Function[a]	Control	24.18	2.70
	Restricted	23.66	3.85
Response Initiation[b]	Control	15.94	11.79
	Restricted	26.95	22.94
Divergent Thinking[c]	Control	1.59	1.70
	Restricted	2.50	2.30
Response Inhibition[d]	Control	2.71	2.80
	Restricted	3.68	3.41
Cognitive Flexibility[e]	Control	15.41	3.45
	Restricted	13.78	5.13
Rule Attainment[f]	Control	6.00	1.12
	Restricted	6.56	1.73
Sustained Attention[g]	Control	1.75	2.64
	Restricted	10.16	10.74
Working Memory[h]	Control	75.00	25.49
	Restricted	69.54	26.15

Note. Sleep Restricted participants (n=120) had four hours time in bed for sleep for five consecutive nights. Control participants (n=17) had ten hours time in bed for sleep for five consecutive nights.
[a] Hayling and Brixton sum of scaled scores; [b] Hayling part B latency; [c] Hayling category 'B' errors; [d] Hayling sum of 'A' and 'B' errors; [e] Brixton errors; [f] Brixton scaled score
[g] PVT lapses; [h] N-back percent correct

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Table 5
T-tests for Between Groups Differences on Executive Function Measures

Executive function measure	*t*	*df*	*p*
Overall Executive Function[a]	-0.53	134	*ns*
Response Initiation[b]	3.10*	36	.00
Divergent Thinking[c]	1.97	25	.06
Response Inhibition[d]	1.30	23	*ns*
Cognitive Flexibility[e]	-1.26	134	*ns*
Rule Attainment[f]	1.79	28	.08
Sustained Attention[g]	6.94*	96	.00
Working Memory[h]	-0.76	124	*ns*

Note. Sleep Restricted participants (n=120) performed significantly worse than controls (n=17) on measures of response initiation and sustained attention. There was a trend for poorer performance in the sleep restricted group relative to controls on measures of divergent thinking and rule attainment.
[a] Hayling and Brixton sum of scaled scores; [b] Hayling part B latency; [c] Hayling category 'B' errors; [d] Hayling sum of 'A' and 'B' errors; [e] Brixton errors; [f] Brixton scaled score
[g] PVT lapses; [h] N-back percent correct
*significant at $p < .01$

Figure 1: Scatter plot with linear regression line for Overall Executive Function by SWS

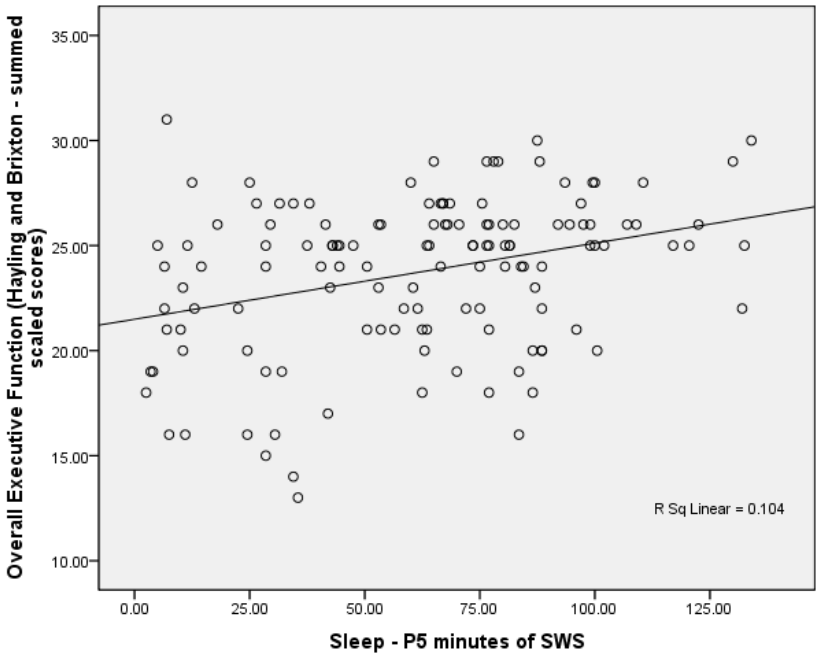

Figure 2: Scatter plot with linear regression line for Response Initiation by SWS

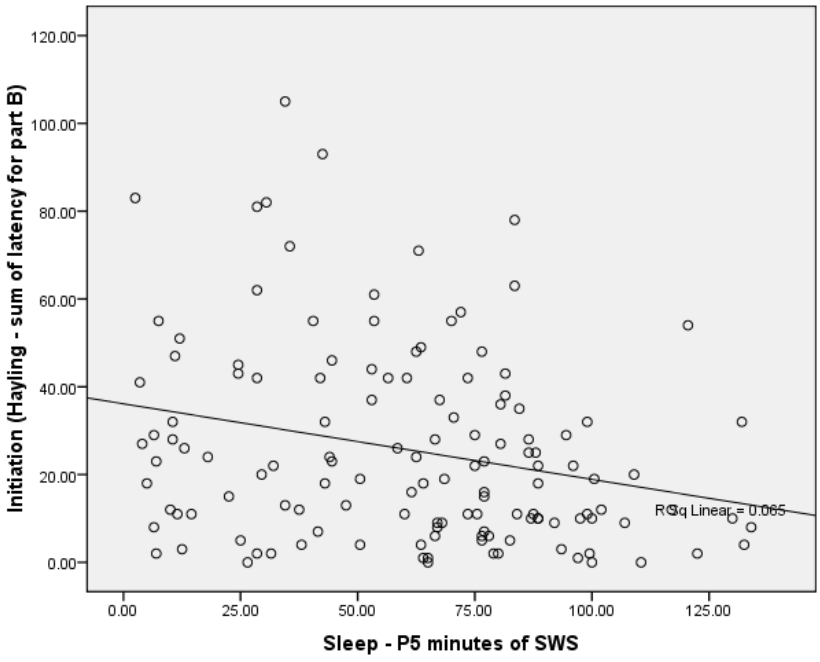

Figure 3: Scatter plot with linear regression line for Response Inhibition by SWS

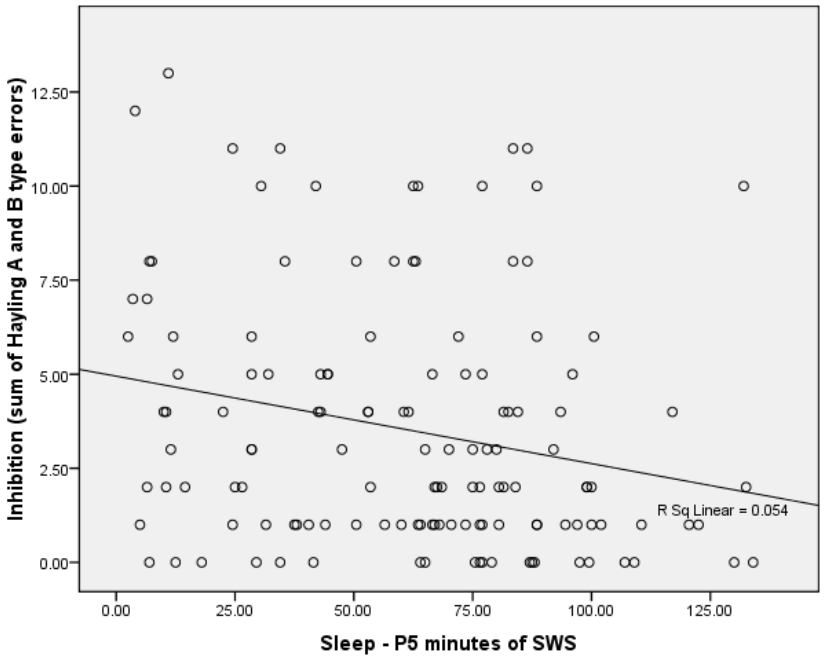

Figure 4. Scatter plot with linear regression line for Divergent Thinking by SWS

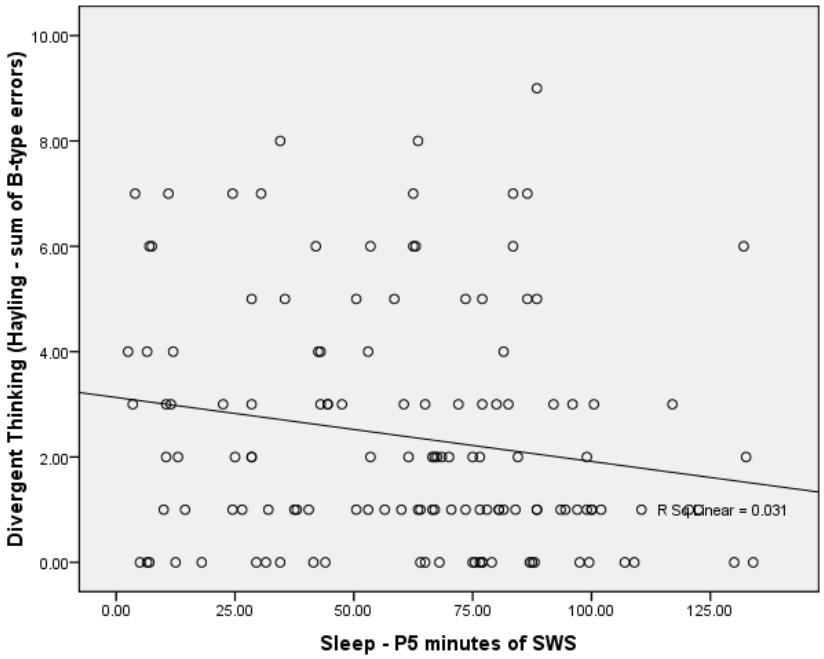

Figure 5. Scatter plot with linear regression line for Cognitive Flexibility by SWS

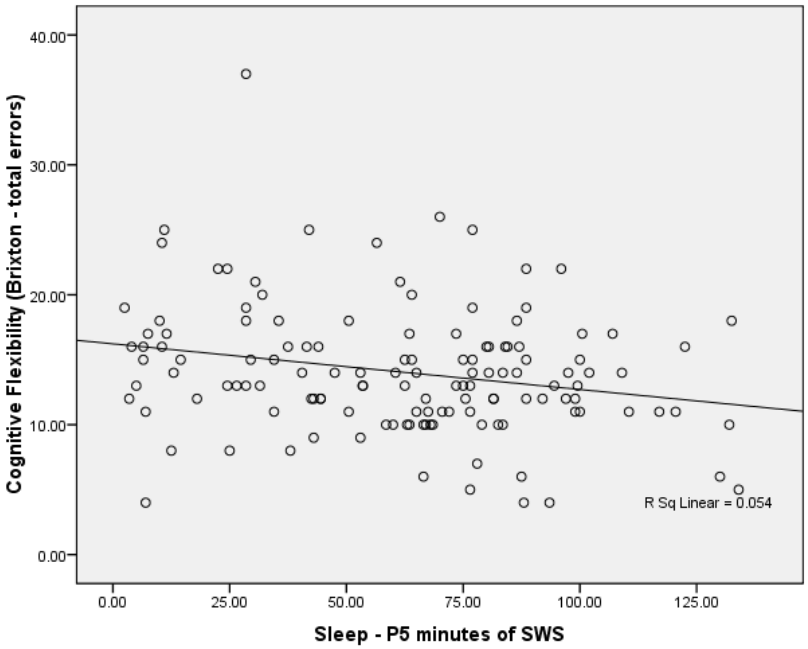

Figure 6. Scatter plot with linear regression line for Rule Attainment by SWS

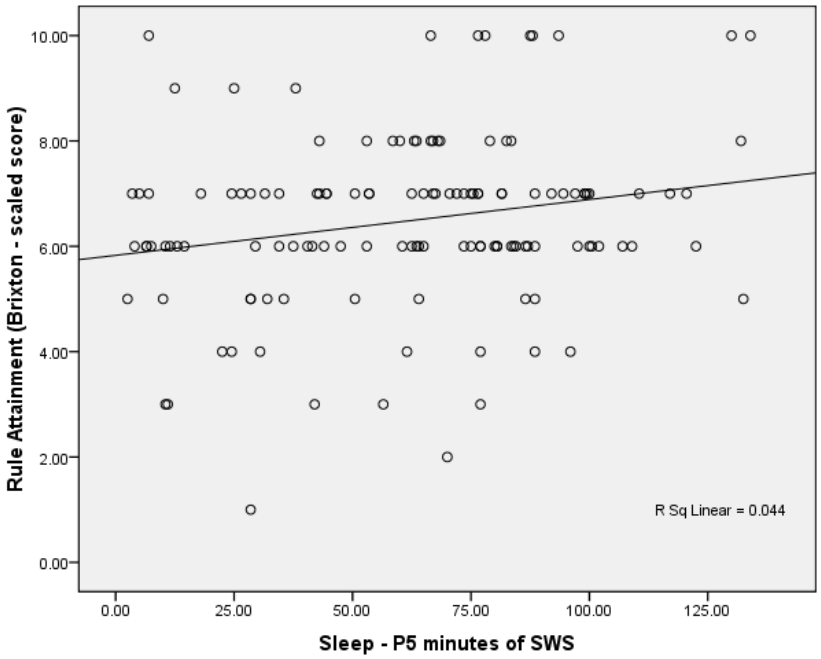

Figure 7. Scatter plot with linear regression line for Sustained Attention by SWS

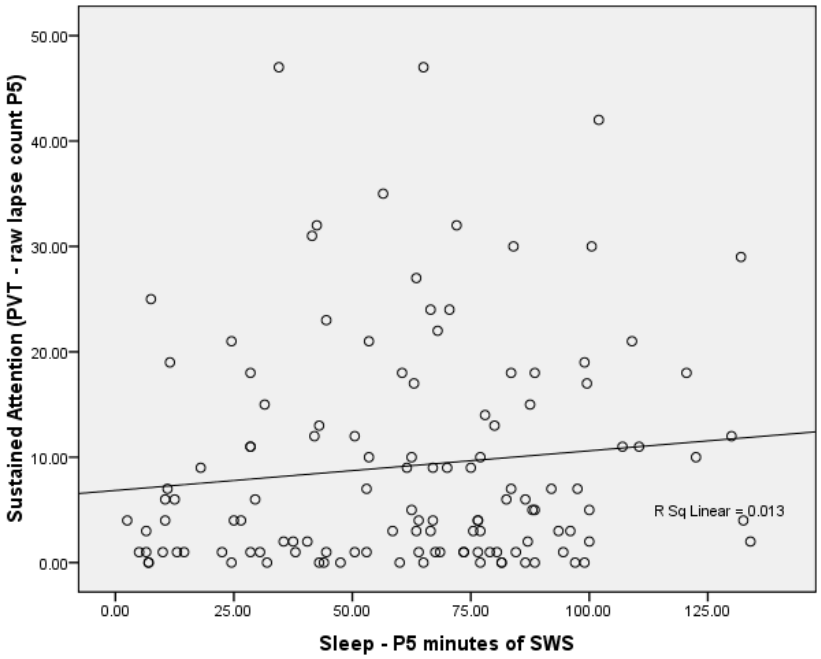

Figure 8. Scatter plot with linear regression line for Working Memory by SWS