The Relationship Between Sleep and Performance on Tests of Pattern Separation and the Cambridge Neuropsychological Test Automated Battery (CANTAB)

by

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B.A. (Hons.), Thompson Rivers University, 2021

Thesis Submitted in Partial Fulfillment of the
Requirements for the Degree of
Master of Arts

in the
Department of Psychology
Faculty of Arts and Social Sciences

SIMON FRASER UNIVERSITY
Fall 2023

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Abstract

Sleep disturbances are considered both a risk factor for and symptom of Alzheimer's disease (AD). To identify sleep-dependent cognitive tests, we monitored rest and activity patterns for 7 days in younger (N=89, 18-30 years) and older (N=40, 50-100 years) adults. We then assessed the effects of 24-hour sleep deprivation in sleep-deprived (N=16, 18-40 years) and rested (N=32, 18-40 years) participants. Cognitive performance assessments included the Mnemonic Similarity Task (MST) and CANTAB. We observed a stronger, but not statistically significant relationship between sleep quantity and MST performance in the older adults compared to the younger adults, and statistically significant relationships between performance on the CANTAB DMS and sleep quality in the older adults. In Study 2, the sleep-deprived participants showed poorer MST performance and longer DMS response latencies than rested participants, but relationships were not statistically significant. Sleep-dependent cognitive tests could be used as clinical trial outcome measures for sleep-promoting treatments.

Keywords: Sleep; cognitive performance; CANTAB; pattern separation; Alzheimer's disease

Acknowledgements

I would like to express my sincere appreciation for the wonderful support and invaluable guidance provided by my supervisor, Dr. Brianne Kent, throughout the course of this research. Her dedication and mentorship have been instrumental in shaping my academic and personal growth. I am truly fortunate to have such a fantastic mentor who not only provided me with the necessary resources but also inspired me to push my boundaries.

I would also like to extend my sincere appreciation to Dr. Ralph Mistlberger who has provided wonderful support, lent study materials to the lab, provided advice on how to analyze clockdata, on how to move forward in the data analyses, and provided helpful feedback on thesis progress. I am very grateful to have Dr. Mistlberger on my committee.

I am also extremely grateful for all the assistance with data collection and analysis that I have received from research assistants and colleagues; Devan Gill, Robert Gibson, Kashish Mehta, Julia Mugliston, Arman Virk, Liliane Tansley, Vanessa Salzano, Tina Shehata, Hannah Chute, Japneet Kaur, Olivia Braziller, Saba Shafigh, Nora Backlund, Taha Yildirim, Sara Tam, and Alex Nash. This research would not have been possible without their hard work and dedication. I would also like to extend my thanks to all the research participants who have taken the time to participate.

I have been enjoying working in the Translational Neuroscience Lab (TNL) and working with my amazing lab members. Their friendship, unwavering support, and humor have made my research journey not only productive but also enjoyable and have enriched my graduate experience. I am grateful to have had the privilege of working alongside the lab's supportive members.

Last, but not least, I would like to thank my parents in Norway, Vigdis and Sven Roenningen, for always supporting and believing in me.

Thank you all!

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List of Abbreviations

Aβ	Beta-amyloid
AD	Alzheimer's disease
APP	Amyloid precursor protein
BDNF	Brain derived neurotrophic factor
BF	Basal forebrain
CANTAB	Cambridge Neuropsychological Test Automated Battery
CSF	Cerebrospinal fluid
DG	Dentate gyrus
DMS	Delayed Matching to Sample
DMSML	Delayed Matching to Sample Mean Correct Latency
DMSMLAD	Delayed Matching to Sample Mean Correct Latency (All Delays)
DMSMLS	Delayed Matching to Sample Mean Correct Latency (Simultaneous)
EC	Entorhinal cortex
EEG	Electroencephalography
GABA	Gamma-aminobutyric acid
ipRGCs	Intrinsically photosensitive ganglion cells
ISF	Interstitial fluid
LC	Locus coeruleus
LDI	Lure discrimination index
MCI	Mild cognitive impairment
MoCA	Montreal Cognitive Assessment
MOT	Motor Screening Task
MST	Mnemonic Similarity Task
MTL	Medial temporal lobe
NREM sleep	Non-rapid eye movement sleep
PAL	Paired Associates Learning
PALFAMS	Paired Associated Learning First Attempt Memory Score
PALMETS	Paired Associated Learning Mean Errors to Success
PALTEA	Paired Associated Learning Total Errors (Adjusted)
PGO-waves	Ponto-geniculo-occipital (PGO) waves
PSG	Polysomnography
PVT	Psychomotor Vigilance Task

REC	Recognition memory
RHT	Retinohypothalamic tract
REM sleep	Rapid eye movement sleep
RTI	Reaction Time Inventory
RTIFMMT	RTI Mean Five-Choice Movement Time
SCN	Suprachiasmatic nucleus
TMN	Tuberomammillary nucleus
SWM	Spatial Working Memory
SWMBE	Spatial Working Memory Between Errors
SWMS	Spatial Working Memory Strategy (6-8 Boxes)
SWS	Slow-wave-sleep
VLPO	Ventrolateral preoptic area
WASO	Wake after sleep onset

Chapter 1.

Introduction

We spend approximately ⅓ of our lifetime asleep (Institute of Medicine, 2006). Sleep is defined as an inactive, natural, and reversible state of diminished reactivity to extrinsic stimuli (Rasch & Born, 2013). The timing, depth and duration of sleep are regulated by the interaction between a homeostatic control termed process S (i.e., duration of prior wakefulness), and the time-of-day termed process C (i.e., circadian control) (Borbély, 1982). During sleep, we shift between different sleep stages. The shifts between sleep stages are described as our sleep architecture, which is the basic organization of sleep (Colten & Altevogt, 2006; Carskadon & Dement, 2011). The sleep stages consist of rapid eye movement (REM) and non-rapid eye movement (NREM) sleep. REM is characterized by the occurrence of rapid eye movements, higher dreaming frequency, increased heart rate, muscle atonia (i.e., paralysis or loss of muscle tone), and desynchronized brain wave activity (theta; 4-8 Hz) shown by electroencephalography (EEG) measures (Carskadon & Dement, 2011). In contrast, NREM is a different sleep form divided into N1, N2, and N3 sleep stages (Saper et al., 2005; Colten & Altevogt, 2006; Dijk et al., 1999). The NREM stage N1 involves sleep initiation, whereas N2 includes sleep spindles (i.e., bursts of rhythmic sigma waves of 12-14 Hz) and k-complexes (i.e., distinct high-voltage, biphasic waves lasting longer than 0.5 s). The N2 stage indicates that sleep has taken place (Carskadon & Dement, 2011). The last NREM sleep stage N3 is characterized by lower heart rate, slower breathing, and is the most challenging sleep stage to be woken up from. The N3 stage is defined by slow-wave-sleep (SWS) marked by high-voltage slow wave activity (i.e., delta waves; 1-4 Hz).

Across the night, we cycle between NREM and REM sleep stages and the average length of this cycle is approximately 90 - 110 min (Carskadon & Dement, 2011). During the initial cycle, the REM period lasts for approximately 1 to 5 min, however, becomes longer in duration later in our sleep cycle. We experience the highest amount of REM in the last part of our sleep episode (Carskadon & Dement, 2011; Saper et al., 2005). The NREM stage N1 lasts for approximately 1 to 7 min, whereas the N2 stage

lasts for approximately 10 to 25 min in the initial cycle. N2 becomes longer in duration with each cycle, accounting for approximately 50% of total sleep time (Colten & Altevogt, 2006). N3 is regulated homeostatically meaning that it is associated with the amount of time spent awake (sleep debt build-up), and we experience the highest amounts of N3 during the first part of the night (Carskadon & Dement, 2011). N3 lasts for approximately 20 to 40 min during the early sleep cycles (Colten & Altevogt, 2006). As the homeostatic drive for sleep declines (Taillard et al., 2003), the N3 stage takes place to a lesser extent and lighter NREM sleep stages (i.e., N2) and REM sleep predominate (Carskadon & Dement, 2011). On average, NREM sleep accounts for approximately 75 to 80 percent of our total sleep time, whereas REM sleep represents 20 to 25 percent of the total time asleep (Carskadon & Dement, 2011).

1.1. Neural circuitry involved in circadian rhythms, wakefulness, and sleep

The hypothalamus contains subregions involved in regulating the sleep-wake cycle (Ma & Morrison, 2023; Brown et al., 2012; Saper et al., 2005). An integral neural structure included in the hypothalamus and contributing to the control of this sleep-wake cycle includes the suprachiasmatic nucleus (SCN). The SCN is a bilateral structure located in the anterior part of the hypothalamus on each side of the third ventricle and above the optic chiasm. A major tract of the SCN includes the monosynaptic retinohypothalamic tract (RHT), which arises from the retina's intrinsically photosensitive ganglion cells (ipRGCs). The ipRGCs contain the specialized photopigment *melanopsin,* which absorbs light. Briefly, RHT input synchronizes core clock genes in SCN neurons, and the coupling of these clock genes further entrain circadian oscillators in other brain regions and bodily tissues (Abe et al., 2002). Thus, the SCN receives input about light exposure directly from our eyes and plays an integral part in controlling our sleep-wake cycle and circadian rhythms by utilizing the light-dark cycle. External (e.g., light during the light cycle) and internal (e.g., melatonin during the dark cycle) timing cues have strong influences on this circadian clock, and are referred to as *zeitgebers* (Scammel et al., 2017). These zeitgebers aid the SCN in coordinating different cellular clocks across the body involved in various processes such as temperature regulation and circadian feeding rhythms.

1.1.1. Wakefulness

The SCN projects efferent signals to the brain stem, which contributes to the control of sleep-wake transitions (Scammell et al., 2017; Moore, 2007; Saper et al., 2005). The waking state is maintained by wake promoting signals mediated by an ascending arousal pathway originating in the rostral pons and running through the brainstem and midbrain reticular formation. These signals are projected to the basal forebrain and the cerebral cortex as well as to the entire forebrain. The brainstem includes the locus coeruleus (LC) producing forebrain norepinephrine, the raphe nuclei producing serotonin, and the laterodorsal tegmental and pedunculopontine nucleus producing acetylcholine (Breton-Provencher et al., 2021; Schwartz & Roth, 2008). The midbrain includes the ventral tegmental area producing dopamine. These neurotransmitters are important for wakefulness. Other neurotransmitters important for wakefulness include orexin, histamine, and glutamate (Falup-Pecurariu et al., 2021; Scammel et al., 2017). Orexin, produced by the lateral hypothalamus, activates neurons in the tubero-mammillary nucleus (TMN), dorsal raphe nucleus, thalamus, and LC (Falup-Pecurariu et al., 2021; Scammel et al., 2017). Histamine is produced by the posterior hypothalamic TMN, and is projected to the thalamus, which also is involved in wakefulness (Scammel et al., 2017; Falup-Pecurariu et al., 2021). Glutamate, gamma-aminobutyric acid (GABA), and acetylcholine, produced by basal forebrain (BF) cholinergic neurons, directly project to the cortex and promote the waking state. Thus, the waking state depends on input from multiple activating systems (see Fig. C.1 in Appendix C).

1.1.2. Sleep: NREM and REM

The SCN projects efferent sleep-promoting signals to the pineal gland, which is located within the brain's two hemispheres (Ma & Morrison, 2023; Scammell et al., 2017). Upon receiving these signals from the SCN, the pineal gland produces the hormone melatonin, only at night. In humans, melatonin is integral for sleep onset and maintenance, and for annual rhythms. The ventrolateral preoptic area (VLPO) in the hypothalamus also contributes to the sleep onset and maintenance process (see Fig. C.1 in Appendix C). Specifically, the VLPO projects GABAergic signals to arousal-promoting brain regions such as the ascending arousal system, the TMN, and the LC (Falup-Pecurariu et al., 2021; Moore, 2008; Schwartz & Roth, 2008). The VLPO has

been described as a flip-flop switch. Specifically, during NREM sleep, produced by the thalamic reticular nucleus and cortex, it sends GABAergic projections to arousing regions (e.g., TMN and LC). During wakefulness, the VLPO is also in turn inhibited by these arousal systems, and the flip-flop switch is stabilized by orexinergic neurons of the lateral hypothalamus. The VLPO is important for NREM sleep promotion (Scammel et al., 2017) as it contains NREM sleep-active neurons (Alam et al., 2014). Furthermore, adenosine, released by neural activity such as the basal forebrain cholinergic cells during prolonged wakefulness, also supports our homeostatic sleep drive. This increase of extracellular adenosine decreases activity of these cholinergic wake-promoting cells (Saper et al, 2005; Porkka-Heiskanen, 1999). Adenosine is one of the *somnogens* (i.e., sleep-promoting substances) that mediate NREM sleep following long periods of wakefulness, associated with sleep debt build up (Scammel et al., 2017).

REM sleep regulation and atonia are regulated by brainstem regions such as the pons, medulla, and the midbrain (Brown et al., 2013). REM sleep initiation is regulated by signaling between cholinergic neurons and also aminergic neurons, which produce histamine, serotonin and norepinephrine (Deak & Stickgold, 2010). Aminergic neurons, such as serotonergic and noradrenergic neurons, are inhibited during REM, whereas cholinergic neurons are active (Walker & Stickgold, 2004). Glutamatergic neurons in the pons may also be important in generating REM sleep (Brown et al., 2013). REM is associated with the production of ponto-geniculo-occipital (PGO) waves, which are phasic endogenous wave forms located in the pons, the lateral geniculate nuclei of the thalamus, and the occipital cortex. Furthermore, neurons in the pons, LC, and ventromedial medulla send efferent signals to the glycinergic spinal motor neurons in the spinal cord and the muscles to inhibit muscle activity during REM sleep, thus establishing atonia (i.e., loss of muscle tone) (Falup-Pecurariu et al., 2021; Scammel et al., 2017). Consequently, this prevents dreaming enactment during REM, which is the sleep stage when our dreams become more vivid. However, muscular tone-muscle twitches observed during rapid eye movements occur due to brief interruptions in the muscular atonia (Falup-Pecurariu et al., 2021).

1.2. How can sleep and wakefulness be measured in human research?

Researchers use both objective and subjective measures to study sleep processes in-lab and in the home environment. Assessment tools may influence findings and interpretations in studies investigating the effects of sleep, which is why it is important to understand how various sleep assessment methods differ (Lehrer et al., 2022).

Subjective sleep assessments include sleep diaries and questionnaires. Sleep diaries are a widely used sleep assessment method for collecting data on sleep and wake times as well as number, duration and reasons for nocturnal awakenings (Buysse et al., 2006). Moreover, use of sleep diaries is considered the gold-standard of self-reported sleep duration, and can be a feasible and efficient means of collecting sleep data, particularly in studies including larger sample sizes (Mallinson et al., 2019). However, sleep diaries depend on research participants' sustained compliance (Thurman et al., 2018). Additionally, sleep quality and quantity may be over-reported in sleep diaries (Van Den Berg et al., 2008), and the diaries may incur participant burden as they often are time consuming and tedious (Lehrer et al., 2022). Therefore, researchers often use multiple modalities including subjective and objective sleep measures to gather data where subjective measures including sleep diaries might fail, and vice versa (Lehrer et al., 2022).

Polysomnography (PSG) is the gold-standard for objectively assessing sleep and sleep architecture (Mallinson et al., 2019). PSG records EEG, blood oxygen levels, breathing and heart rate in addition to leg and eye movements during sleep (Rundo & Downey, 2019). However, the method may be time consuming, incur participant burden, and include a high cost and access challenges (Walia & Mehra, 2019; Van de Water et al., 2011). An alternative objective approach to indirectly assess sleep includes wrist actigraphy, which was originally developed as a means to estimate sleep parameters over a number of nights in the home environment (Smith et al., 2018). Wrist actigraphy measures naturalistic rest and activity patterns and can be used to collect data non-invasively and continuously over days, weeks, or months (Martin & Hakim, 2011; Ancoli-Israel et al., 2003; de Souza et al., 2003; Smith et al., 2018; Sadeh & Acebo, 2002). Actigraphy has low burden (e.g., participant and caregiver burden) and is recommended

in studies assessing sleep in the home environment (Lehrer et al., 2022). It is validated with PSG, showing similarity rates of above 80% of total sleep time, sleep efficiency, nocturnal awakenings, sleep onset latency, and wake after sleep onset (WASO) (de Souza et al., 2003; Cole & Kripke., 1992; Lichstein et al., 2006; Marino et al., 2013; Sadeh, 2011; Kushida et al., 2001; Acebo et al., 2006; Ancoli-Israel et al., 2003.). However, in periods of time with low activity such as when watching TV or reading, actigraphy may show weak sensitivity for distinguishing between sleep and wakefulness (Gao et al., 2022; Kushida et al., 2001). Additionally, actigraphy may also underestimate sleep latency and nocturnal awakenings, and overestimate total sleep time and sleep efficiency (de Souza et al., 2003), especially in groups with sleep disorders (Sivertsen et al., 2006; Kushida et al., 2001). Thus, combining different sleep data collection methods, such as actigraphy and sleep diaries, may be more advantageous, informative, and reliable than relying on only one measure alone.

1.3. Sleep and aging

Research has shown that sleep and sleep architecture change from young adulthood to older adulthood (Dijk et al., 1999; Li et al., 2018). Adult sleep may include minor and brief nocturnal awakenings, however, the sleep is relatively consolidated and stable (Dijk et al., 1999). However, as humans age, research has found that aging is associated with changes in the sleep-wake homeostasis and the circadian biological clock (Schmidt et al., 2012; Duffy et al., 2002). These changes include advances in the circadian phase leading to a preference in older individuals for waking up and going to bed earlier compared to younger adults (Schmidt et al., 2012; van Someren, 2000; Li et al., 2018). Additionally, studies have found that sleep duration or total sleep time tends to decrease as we get older (Schmidt et al., 2012; Li et al., 2018; Dijk et al., 1999) and older adults may experience more frequent nocturnal awakenings than younger individuals (Li et al., 2018; Ohayon et al., 2004). These changes all affect sleep efficiency, which is the ratio of total sleep time to time in bed, and studies have demonstrated that sleep efficiency shows steady declines after 60 years of age (Ohayon et al., 2004). Moreover, studies using PSG have shown that individuals around 60 years of age and older spend less time in N3 (Dijk et al., 2010; Dijk et al., 1999; Dijk et al., 2000; Swaab et al., 1985) and REM (Mazzotti et al., 2014; Dijk et al., 1999) compared to younger adults. As arousal thresholds are highest during N3, declines in N3 would lead

to lower arousal thresholds, thus more frequent nocturnal awakenings in older individuals (Dijk et al., 2000). Additionally, older individuals experience more frequent shifts between the sleep stages than younger adults (Conte et al., 2014). Reduced and poor nighttime sleep might thus be associated with increased daytime tiredness and daytime napping in older adults (Ohayon et al., 2004; Huang et al., 2002), which also may be due to declined circadian wake-promoting signals during the biological day (Schmidt et al, 2012). Therefore, the age-related reduced homeostatic sleep drive may help explain the fragmented and shorter sleep at night-time, whereas declined circadian wake promotion during the biological day might lead to more frequent daytime naps in the elderly.

1.3.1. Sleep and Alzheimer's disease development

Poor sleep is considered a risk factor for Alzheimer's disease (AD) development and studies have found that there may be a bidirectional relationship between sleep and AD progression (reviewed by Kent et al., 2021; Ju et al., 2014). AD is the most common type of dementia, which is a neurocognitive disorder and an umbrella term for impairment in cognition that interferes with the ability to perform daily activities (5th ed., DSM – 5, American Psychiatric Association, 2013). AD is a progressive neurodegenerative disorder that involves impairments in cognition (e.g., episodic memory, attention, reasoning and language) and behaviour (5th ed., DSM–5, American Psychiatric Association, 2013). Specifically, sleep disruption has been linked to the aggregation of beta-amyloid (Aβ) plaques and tau accumulation in the brains of rodents (Wang & Holtzman, 2020; Roh et al., 2012) and humans (Barthélemy et al., 2020; Shokri-Kojori et al., 2018). These are the pathological hallmarks of AD. Aβ is a soluble 38-43 amino acid peptide formed by proteolytic cleavage (i.e., breaking of the peptide bonds between amino acids in proteins) of the amyloid precursor protein (APP) (Cirrito et al., 2005). Tau is a cytoplasmic microtubule-associated protein working to regulate the maintenance and assembly of microtubules' structural stability (Yamada et al., 2014; Holth et al., 2019). Research suggests that tau hyperphosphorylation is an early marker of tau-mediated neurodegeneration and is linked to tau accumulation intracellularly, leading to synaptic and neuronal decline, neurofibrillary tangles, and cognitive impairment (Barthélemy et al., 2020). Research also suggests that the accumulation of

Aβ leads to the development of extracellular insoluble plaques leading to neurotoxicity and synaptic and neuronal decline (Barthélemy et al., 2020).

In non-pathological conditions, the sleep-wake cycle modulates Aβ and tau levels in the CSF (Xie et al., 2013; Pooler et al., 2013; Yamada et al., 2014; Holth et al., 2019). While awake and active, the brain produces more Aβ and tau compared to when we are asleep (Holth et al., 2019; Ju et al., 2014; Pooler et al., 2013). Specifically, Aβ and tau production and release are regulated by and are a byproduct of synaptic vesicle exocytosis and excitatory activity (Xie et al., 2013; Cirrito et al., 2005; Holth et al., 2019), and leads to increased Aβ and tau levels in the interstitial fluid (ISF) in the extracellular space. Therefore, synaptic activity may be a modulator in neurodegenerative disease processes by influencing Aβ and tau deposition.

Recently, studies have found that tau and Aβ proteins can be cleared out of the brain and into the cerebrospinal fluid (CSF) through a process termed glymphatic clearance (Jessen et al., 2015; Iliff et al., 2012; Jouvencel et al., 2023), also called glial-dependent lymphatic transport (Reddy & van der Werf, 2020). Sleep, and particularly the N3 stage, has been demonstrated to increase glymphatic clearance processes (Reddy & van der Werf, 2020). Specifically, N3 including slow oscillatory EEG increases glymphatic clearance by producing an CSF flux within the interstitial cavities in the extracellular space (Fultz et al., 2019). In addition, during sleep, norepinephrine levels decline, which expands extracellular space in the brain, resulting in reduced fluid flow resistance. Then, CSF circulates through the brain, interchanging with ISF and clears metabolic waste products (e.g., Aβ). This leads to interstitial clearance by facilitating CSF infiltration (Jessen et al., 2015). The exchange between ISF and CSF takes place around the cerebral vasculature, more specifically, with CSF influx around arteries, while the ISF exits along the veins (Iliff et al., 2012).

During wakefulness, the glymphatic clearance system is largely disengaged (Jessen et al., 2015). Research has shown that sleep deprivation may increase Aβ and tau levels (due to less glymphatic clearance and more synaptic activity), whereas sleep and particularly N3 leads to a reduction in these levels (Ju et al., 2014; Huang et al., 2012; Jouvencel et al., 2023). This suggests that higher levels of sleep and glymphatic clearance may be protective against AD.

When metabolic waste products (e.g., tau and Aβ) accumulate in the brain and nervous system as a consequence of poor sleep, this can also have negative effects on sleep quality and quantity, underlining the bidirectional relationship. Specifically, as Aβ accumulates, this may lead to further sleep disruptions due to Aβ's negative effects on sleep-promoting regions in the brain (Ju et al., 2014). In symptomatic AD, patients report sleep-wake abnormalities such as excessive daytime sleepiness due to fragmented and disrupted nocturnal sleep, delayed bed and wake times, sundowning (i.e., confusion and agitation occurring in the late afternoon and lasting into nighttime) and reduced sleep efficiency (Ju et al., 2014). As AD progresses, these sleep-wake abnormalities are aggravated leading to a vicious cycle of tau and Aβ accumulation and struggles with sleep, in addition to further declines in cognitive functioning, such as memory (Ju et al., 2014).

Research has found that sleep disruptions often precede AD diagnosis by several years and may be present before cognitive deterioration (Lloret et al., 2020; Zhang et al., 2019; Ju et al., 2014). For example, Lim et al. (2013), found that participants with fragmented sleep were 1.5 times more likely to develop AD compared to those with normal sleep in a 6-year follow-up period. In a longitudinal epidemiological study, the authors identified cognitive impairment one year later in participants who had poor sleep quality at the time of testing (Potvin et al., 2012). In pre-symptomatic stages of AD, reductions of $A\beta_{42}$ have been detected in CSF, indicating reduced glymphatic clearance (Ju et al., 2014). Therefore, sleep abnormalities may increase soluble Aβ over the long term, leading to higher chance of Aβ plaque aggregation, and subsequently, symptomatic AD. This suggests that sleep disruptions may influence or exacerbate AD pathology and that sleep improvement may work against this development (Wennberg et al., 2017; Ju et al., 2014). As sleep and particularly N3 continues to decline in AD shown by EEG (Westerberg et al., 2012), sleep could be used as a therapeutic target in those at risk of and in those with AD.

1.4. Sleep and cognition

Sleep has been shown to influence cognitive functions such as memory processes, learning (Alhola & Polo-Kantola, 2007; Rasch & Born, 2013; Westerberg et al., 2012; Deak and Stickgold, 2010), and also executive functions, which include attentional processes (e.g., sustained attention), working memory (i.e., manipulation of

temporarily stored information) and inhibitory control (i.e., resisting impulsive actions) (Diamond, 2013).

Memory processes involve non-declarative and declarative memory processes (Deak & Stickgold, 2010). Non-declarative or implicit memory cannot be retrieved to conscious awareness and includes for example procedural memory, which helps performance of various tasks and movements (Squire & Zola-Morgan, 1996). Declarative memory, on the other hand, can be recalled to conscious awareness (Squire & Zola-Morgan, 1996). This form of memory encompasses episodic memory, which is memory for specific life events, and semantic memory, including memory for factual information and general knowledge. Episodic memory, a term introduced by Endel Tulving in 1972, refers to memory for past personal experiences and events and the temporal-spatial relations among these events and experiences (Tulving, 1972; Aly & Moscovitch, 2010). These memory processes depend on the hippocampus, which is located in the medial temporal lobe (MTL) (Squire & Zola-Morgan, 1996).

The hippocampus has been found to be involved in memory consolidation, particularly declarative memory processing, during sleep (Inostroza & Born, 2013; Ellenbogen et al., 2006; Poh & Cousins, 2018; Diekelmann, 2014). Specifically, slow-wave sleep (SWS) is hypothesized to reactivate and strengthen recently encoded hippocampal representations of experienced events and integrate the representations into long-term memory (Inostroza & Born, 2013; Rasch & Born, 2013).

When sleep is restricted or disturbed, cognitive abilities, such as memory processes, tend to decline (Mantua & Simonelli, 2019). This may have detrimental consequences in everyday life, such as in different occupations requiring high alertness, for example in emergency and medical services. Therefore, it is important to understand the relationship between sleep and cognitive performance. In the next chapter, we will look closer at the role of sleep in different cognitive processes.

Chapter 2.

Exploring the relationship between sleep and cognitive performance

2.1. Sleep's role in episodic memory, pattern separation, and the Mnemonic Similarity Task

Poor sleep quantity and quality have been frequently associated with episodic memory impairments (Kent & Mistlberger, 2017; Hokett et al., 2021). Episodic memory processes, for example encoding and consolidation, rely on different parahippocampal regions including the entorhinal cortex (EC) and hippocampal areas such as the perforant path, the dentate gyrus (DG), and the CA3 (Kent & Mistlberger, 2017; Leutgeb et al., 2007). Episodic memory processes also rely on hippocampal neurogenesis, which is the formation of new neurons in the subgranular zone, located between the granule cell layer and hilus of the DG (Kempermann et al., 2015).

Hippocampal neurogenesis is the mechanism behind a computational process called pattern separation, which occurs during memory encoding (Marr, 1971; Stark et al., 2019; Norman & O'Reilly, 2003; McClelland et al., 1995; Santoro, 2013; Clelland et al., 2009; Hunsaker & Kesner, 2013; Berron et al., 2016; Bakker et al., 2008; Leutgeb et al., 2007). Pattern separation is uniquely important to episodic memory as it plays an integral part in decreasing possible interference among similar memory representations, and forms separate memories of experienced events and encountered stimuli (Sahay et al., 2011; Stark et al., 2019; Norman & O'Reilly, 2003; Leutgeb et al., 2007). Episodic memory failure might include forgetting an event but it can also be the consequence of confusing similar experiences. Thus, the outcome of effective pattern separation is the ability to discriminate between memories that are similar. Poor sleep has been suggested to impair DG hippocampal neurogenesis, which may have negative effects on pattern separation performance (Kent & Mistlberger, 2017).

Studies have found that sleep before encoding might be crucial for the encoding to be successful (Yoo et al., 2007; Antonenko et al., 2013; Van Der Werf et al., 2009; Cousins et al., 2019) and also enhances pattern separation processes (Poh & Cousins, 2018). For example, it is suggested that sleep and particularly N3 engages in a down-

scaling and desaturation process of synapses that were active during input encoding while awake (Tononi & Cirelli, 2006, 2014; Cousins et al., 2019). Thus, weak synaptic connections may be removed by the downscaling and other synapses may regain the capacity to encode new information in the next wakefulness period. Slow oscillations are important in this process in that they facilitate slow and synchronized neuronal firing, which aids synaptic depression or downscaling instead of potentiation. Therefore, sleep before encoding may also facilitate pattern separation processes in the waking period considering that pattern separation takes place during encoding.

In support of the idea that sleep is important for pattern separation, studies have found that sleep loss may lead to impairments in the ability to establish new episodic memories (Poh & Cousins, 2018; Van Der Werf et al., 2009). Specifically, sleep deprivation may impair various cellular and molecular mechanisms in hippocampal regions that are important for encoding and pattern separation, such as the DG/CA3 (Abel et al., 2013; Inostroza & Born, 2013). For example, sleep deprivation may produce deficits in cell proliferation in the subgranular zone, which may lead to impairments in forming adult-born neurons in the hippocampus (Kent & Mistlberger, 2017). Sleep deprivation might also cause impairments in growth hormones such as the brain derived neurotrophic factor (BDNF), which is an important contributor to neurogenesis (Erickson et al., 2010; Calabrese et al., 2014; Bekinschtein et al., 2013). Thus, cognitive measures that show sensitivity to hippocampal dependent processes (e.g., pattern separation) may be useful in identifying individuals who experience poor sleep quality and quantity.

The Mnemonic Similarity Task (MST) is a validated task designed to measure hippocampal-dependent learning (Stark et al., 2019; Kirwan and Stark, 2007; Bakker et al., 2008; Toner et al., 2009; Holden et al., 2013; Ally et al., 2013; Stark et al., 2013; Bennett and Stark, 2015; Yassa et al., 2010ab, 2011ab; Doxey & Kirwan, 2015; Leal et al., 2019; Stark et al., 2023) and is shown to be sensitive to hippocampal subfield function (particularly in the CA3/DG subfield), and age-related cognitive decline (Stark et al., 2019; Marks et al., 2017). The task was originally developed to mirror tasks used to measure pattern separation performance in rodents, which assessed spatial pattern separation (Stark et al., 2019; Gilbert et al., 1998; Gilbert et al., 2001). Performing the MST yields different memory measures. Two commonly examined measures include the Lure Discrimination Index (LDI or “separation bias”) and Recognition Memory, commonly referred to as REC (Stark et al., 2013; Stark et al., 2019). The LDI measure indicates

whether the participant was able to discriminate lures from repeated images, and thus avoid interference of other similar images (Stark et al., 2019). Failure in indicating lures as “similar” and instead judging lure images as “old” (false alarms) suggests ineffective pattern separation during encoding. Correctly judging lures as “similar” would indicate that pattern separation has taken place at a computational level (Kirwan & Stark, 2007). Compared to REC, LDI has been shown to depend more on the hippocampus, and particularly on the CA3/DG subfield (Bakker et al., 2008; Kirwan & Stark, 2007).

To our knowledge, only a few research studies have investigated sleep’s influence on MST performance (Hanert et al., 2017; Doxey et al., 2018; Davidson et al., 2021; Saletin et al., 2016; Chylinski et al., 2022; Cellini et al., 2020; Cellini, 2023). Both Hanert et al. (2017) and Doxey et al. (2018) showed that following a 9-hour (Hanert et al.) and 12-hour (Doxey et al., 2018) retention interval of either sleep or wakefulness, participants in the sleep conditions exhibited superior MST performance compared to participants who had stayed awake during the day. REC scores in Hanert et al.’s study were higher after sleep, and in Doxey et al.’s study, REC showed no effect of sleep or wakefulness. Cellini (2023) assessed whether nocturnal sleep modulated emotional mnemonic discrimination. Similar to Hanert et al. and Doxey et al., Cellini et al. also included a wake and sleep condition. Participants were tested immediately after encoding, and again following a 12-hour delay. A night of sleep stabilized mnemonic discrimination, regardless of the images’ valence. In addition, the sleep group showed superior pattern separation performance compared to the wake group. REC scores were not different between groups. Furthermore, Saletin et al. (2016) demonstrated that pattern separation scores were lower following a night of sleep deprivation, but were recovered after a nap of 90 min. Saletin et al. also showed that structural morphology of human hippocampal subfields contributed in determining sensitivity to sleep loss and predicted recovery following sleep. Additionally, sleep deprivation reduced LDI scores, which were recovered following a recovery nap. Cellini et al. (2020) and Davidson et al. (2021) also tested the effects of a daytime nap on mnemonic discrimination. In both Cellini et al.’s and Davidson et al.’s studies, the authors found that a nap of 60-90 min did not facilitate either REC or LDI performance compared to wakefulness. Last, Chylinski et al. (2022) examined whether the coupling of spindles and slow waves were linked to early change in cognition and Aβ burden in the brain over a span of 2 years in 100 healthy middle aged and older participants. Participants were also assessed on the

MST at baseline and after 2 years. Participants' showed memory declines at the follow-up testing, and declines were related to onset of sleep spindles. Across these different studies, the focus was to investigate how memory consolidation was affected by a retention interval including daytime wakefulness or nocturnal sleep (Hanert et al., 2017; Doxey et al., 2018; Cellini et al., 2023), how a nap affected encoding (Davidson et al., 2021; Saletin et al., 2016) and consolidation (Cellini et al, 2020), and how 24-hour sleep deprivation (Saletin et al., 2016) or differences in sleep spindle onset (Chylinski et al., 2022) affected encoding. None of the studies looked at *different levels* of sleep quantity and quality before encoding and how differences in sleep quantity or quality may be uniquely related to pattern separation. As sufficient encoding is crucial for pattern separation and sleep is important for encoding (Tononi & Cirelli, 2014), examining how sleep quantity and quality before encoding is associated with pattern separation performance could provide more insight into how sleep may affect pattern separation.

2.2. Cambridge Neuropsychological Test Automated Battery and sleep

The Cambridge Neuropsychological Test Automated Battery (CANTAB) is a validated computerized test battery used to measure cognitive performance (Fray & Robbins, 1996; Sahakian et al., 1988; Robbins et al., 1998; Sahakian & Owen, 1992; Robbins et al., 1994; Sahakian et al., 1990; Blackwell et al., 2004; Sternin et al., 2019; de Jager et al., 2005; O'Connell et al., 2004; Fowler et al., 1997). CANTAB was designed by a group of researchers, including Dr. Barbara. J. Sahakian and Dr. Trevor. W. Robbins, in the 1980's at the University of Cambridge. Their aim was to try to adapt paradigms developed for assessing animal models of Alzheimer's disease so that these tests could be used to test human cognition. The animal paradigms had previously been conducted in primates to establish neural substrates of different cognitive functions, especially those involved in AD (Sahakian, 1988; Sahakian et al., 1990; Robbins et al., 1994; Sternin et al., 2019; Fray & Robbins., 1996; Sahakian & Owen, 1992; Mishkin, 1982; Gaffan, 1974; Petrides, 1987; Olton, 1977; Passingham, 1985; Olton and Pappas, 1979). To adapt these measures, it was necessary to identify ways of varying test demands correctly so that they could measure a range of cognitive functions. The CANTAB battery was the first touch-screen based, computerized cognitive battery. It is non-verbal, which prevents confusion due to language issues. CANTAB has also been

widely used in clinical trials, is portable, can be used both in the lab and home environment, and shows test-retest reliability (Zygouris et al., 2015). In addition, it uses a touchscreen, which is user friendly.

The tests are sensitive to cognitive impairments in addition to progressive decline in patients who are in the pre-symptomatic stages of AD (Fowler et al., 1997; Sahakian & Owen, 1992; Fray & Robbins., 1996; Sternin et al., 2019; Sahakian et al., 1988; Sahakian et al., 1990; Swainson et al., 2001; Lee et al., 2003; Égerházi et al., 2007). Specifically, the test results can aid early detection and diagnosis of AD and can indicate deficits in both frontal and temporal brain regions, such as in the entorhinal cortex (EC), which is a location of early AD (Braak & Braak, 1991). For example, in individuals with prodromal Alzheimer's disease, their performance on one of CANTAB's tests, the Paired Associates Learning task (PAL), which heavily relies on the EC region, was found to predict declines in global cognitive function over the course of 8 months (Blackwell et al., 2004). Additionally, 32 months following the study, 11 of these 43 patients received a probable AD diagnosis. Other tests sensitive to MCI and prodromal AD also include the Delayed Matching to Sample (DMS) test measuring visual recognition memory (Lee et al., 2003; Blackwell et al., 2004), 5-Choice Reaction Time Inventory (RTI) measuring divided attention (Thomas et al., 2019; Saunders & Summers, 2010; Gnoni et al., 2023; Csipo et al., 2003) and Spatial Working Memory (SWM) measuring spatial working memory (Égerházi et al., 2007; Saunders & Summers, 2010; Lenehan, 2016). RTI and SWM have been shown to be sensitive to fatigue (Majer et al., 2008). Last, higher CSF levels of tau have been associated with impairments on PAL and SWM, and both SWM and DMS have been associated with lower CSF $A\beta_{42}$ levels (Nathan et al., 2017). Increases in CSF tau and decreases in CSF $A\beta_{42}$ are biomarkers of AD. We are especially interested in these CANTAB tests (i.e., RTI, SWM, PAL, and DMS) and more information about the tests will follow below.

To our knowledge, only a few studies have examined the effects of sleep and circadian rhythms on CANTAB performance in healthy individuals (Waller et al., 2016; Thomas et al., 2019; Santisteban et al., 2019; Ahmad & Bashir, 2017; Dodds et al., 2011; Oosterman et al., 2009; Csipo et al., 2021) and in patients diagnosed with obstructive sleep apnea (OSA) (Naëgelé et al., 2005; Gnoni et al., 2023) and insomnia (Edinger et al., 2021). Some of the studies have used the tests that we are interested in (Waller et al., 2016; Thomas et al., 2019; Csipo et al., 2021; Gnoni et al., 2023; Naëgelé

et al., 2005). Naëgelé and colleagues (2006) used the CANTAB SWM to examine memory impairments associated with obstructive sleep apnea (OSA) and significantly worse performance was detected in those with OSA compared to healthy controls. In a similar vein, Gnoni et al. (2023) used CANTAB tasks, among others, the PAL, RTI, SWM, and DMS to assess cognitive functions in a group of OSA male patients. The most significant deficits were observed in DMS and RTI performance in the patient group. Waller et al. (2016) assessed cognitive performance in a sample of middle-aged males using the DMS, PAL, and RTI to split the middle-aged male sample into cognitively improved versus cognitively impaired groups. Poor cognitive performance of males from the cognitively impaired group was associated with lower subjective sleep quality. A recently published experiment assessed how daytime sleepiness associated with insomnia influenced cognitive performance using, among other CANTAB tasks, the SWM (Edinger et al., 2021). Insomnia patients exhibited more cognitive impairment on tasks regarded as more complex, such as the SWM. Thomas et al. (2020) investigated disrupted sleep in maritime pilots over a week's period, and used, among other CANTAB tasks, the PAL, the RTI, and the SWM. Despite the finding that the maritime pilots experienced higher sleepiness levels as well as poorer sleep, the pilots did not seem to show weaker cognitive performance compared to the controls, which may be due to compensatory strategies (Thomas et al., 2020). Last, Csipo et al. (2021) conducted a 24-hour total sleep deprivation study in healthy young male participants and used the CANTAB tests SWM, RTI, DMS, and the PAL. The sleep deprivation only affected RTI performance and increased reaction times. Across the different studies, participants' performance on the included CANTAB measures showed sensitivity to different levels of sleep and sleep loss, and in some groups (e.g., OSA patients) more than others (e.g., maritime pilots). Investigating how sleep is uniquely sensitive to performance on the tests mentioned would provide more insight into how sleep is uniquely related to cognitive performance on these tests.

Cognitive measures that are sensitive to sleep quality or quantity may be highly valuable in clinical settings. Additionally, researchers are now focusing more on the importance of sleep as a potential therapeutic target for neurodegenerative and neurological diseases and other different physiological conditions. To assess the effect of sleep-targeting therapeutics, suitable cognitive assessments are needed as the assessments used today are tedious and inconvenient (e.g., polysomnography). More

specifically, these cognitive tests can help identify patients and/or other individuals who experience sleep disturbances and who may need therapies focusing on improving sleep. In addition, the tests may be helpful in clinical trials as outcome measures when measuring the efficiency of sleep-promoting interventions and how these interventions might aid cognitive functioning.

Here, we examined the relationship between sleep patterns and different cognitive functions using a variety of cognitive tests including the MST and CANTAB. We used the 5-min NASA Psychomotor Vigilance Task (NASA-PVT) as a positive control measure, because it has been previously shown to be sensitive to sleep loss and circadian misalignment (Dinges & Powell, 1985; Lim & Dinges, 2008). We also assessed how different circadian parameters correlated with the cognitive measures using Clocklab. We were particularly interested in measures that tax pattern separation performance (i.e., MST and CANTAB's Delayed Matching to Sample test), which is novel, and also CANTAB tests designed to detect AD-associated cognitive impairments. To investigate the effects of sleep on cognitive functions measured with these tests, we first conducted an exploratory and correlational study on sleep and cognition in university students and older adults. The exploratory nature of the study allowed us to look at many sleep and cognitive variables. University students frequently experience sleep disruptions, which can have negative impacts on cognition (Schlarb et al., 2017). In addition, sleep disturbances in older adults are common (Li et al., 2018; Ohayon et al., 2004). As sleep changes have been shown to precede the development of cognitive symptoms in AD patients (Ju et al., 2014), recruiting a sample of older adults provides more insight into the relationship between sleep and cognition in older age. We predicted that sleep measures would be most correlated with the cognitive test scores representing pattern separation (i.e., LDI) and CANTAB DMS sub-measures. We also predicted a stronger relationship between sleep and cognitive performance in the older adults compared to the younger adults, and that the younger adults would show better performance on the different cognitive tests (MST and CANTAB) compared to the older adults.

2.3. Methods

2.3.1. Research subjects

The study was approved by the Research Ethics Board (REB) at Simon Fraser University (SFU) (Protocol #30000539). Subjects were 89 undergraduate SFU students recruited via the Research Participation System (sona-systems.com) and through advertisements and payment, and 40 middle-aged and older adults recruited via posters, word-of-mouth, social media platforms and the online platform REACHBC, from the lower mainland and Kamloops. Prior to any testing, participants completed an online consent form and Subject Information Survey, which collected demographic information as well as information about mental, neurological and physical health. We recruited SFU students who were between 18 - 30 years of age and middle-aged and older adults who were older than 50 years of age. Most of the middle-aged and older adults (i.e., 87.7% or 35/40) had more than 12 years of education (16.75 years ± 3.77) compared to the younger participants, where many were in the first year of their programs. The older adults also completed the Montreal Cognitive Assessment duo (MoCA duo) (M = 24.62 ± 2.75; Nasreddine et al., 2005) administered on an iPad (OS 15.4.1, model A2602), with a 260.6 x 174.1 mm screen size.

Both younger and older participants needed to be able to understand and follow written and verbal instructions in order to be eligible to participate. Upon study completion, the participants were thanked and the young adults were compensated with 4 RPS credits or $30, whereas the middle-aged and older adults were compensated with $50.

2.3.2. Procedure

Participants were scheduled for two visits. All visits took place between 10:00 am and 3:00 pm, and participants were able to choose a timeslot that would work best for them to participate. During the first visit, participants met with a member of the study team, went over a second consent form and study instructions, and were provided with an actigraphy watch. Participants were asked to sleep normally at home over 7 consecutive days and filled out a sleep diary every morning. On the 7th day, participants returned to the lab to complete cognitive testing. A step-by-step study guide

standardizing data collection, including scripts, instructions, set-up, and order of procedures, was followed by the experimenter during every test session.

2.3.3. Sleep Assessments: Actigraphy watches and sleep diaries

An actigraphy watch is a lightweight wrist-worn device that measures activity levels, internal and external temperature, and light exposure (Condor Instruments, ActTrust model AT0503). Participants were asked to press an event button when going to bed and when waking up in the morning. The data collected by the watches were used to assess the subjects' bedtime and wake-up time, total sleep time, sleep onset latency, WASO, sleep efficiency, and the number of nocturnal awakenings.

The sleep diaries were hosted by Qualtrics (Qualtrics XM // The Leading Experience Management Software) and the link was sent to the participants via email (See Appendix D). The diaries were used to assess participants' subjective sleep quality and patterns, including questions about the number of awakenings during the night, bedtime and wake-up time, experienced sleep disruptions, approximate total sleep time, and if any, the number of naps, among others. The sleep diary was completed every morning for the previous night over the 7 consecutive days. The sleep diaries were useful when analyzing the actigraphy data in that they provided an additional and subjective measure of bedtime and get-up time, sleep quality (e.g., whether the participant had trouble sleeping or had a full night of sleep), how long it took to fall asleep, among others (Wei et al., 2021).

2.3.4. Cognitive testing

NASA-PVT

The PVT is a simple reaction time assessment that is designed to detect the effects of sleep loss and circadian misalignment (Dinges & Powell, 1985; Lim & Dinges, 2008). The test is a frequently used test to measure sustained attention and reaction time (Dinges & Powell, 1985; Wilkinson & Houghton, 1982; Dorrian et al., 2005; Arsintescu et al., 2017), and is based on a simple visual RT test apparatus originally developed by Wilkinson and Houghton (1982). The PVT has been shown to be highly sensitive to the effects of sleep and sleep loss (Dinges & Powell, 1988; Van Dongen et al., 2003; Belenky et al., 2003; Lim & Dinges, 2008). We used the 5-min NASA PVT,

which has been validated against the 10-min PVT (Lamond et al., 2008; Loh et al., 2004; Roach et al., 2006; Honn et al., 2015; Thorne et al., 2005; Lamond et al., 2005; Thompson et al., 2022; Arsintescu et al., 2017; Arsintescu et al., 2019) and is suitable for touch-screens (Arsintescu et al., 2017, 2019).

The task was presented on an iPad (OS 15.4.1, model A2602), with a 260.6 x 174.1 mm screen size, and participants held the iPad in their hands in a horizontal position, as that has been shown to be preferred by participants and leads to faster reaction times and fewer lapses (Arsintescu et al., 2017). The iPad was set in airplane mode and participants could not see the clock time on the iPad during testing.

The participants were instructed to attend to a small rectangular area on the dark iPad screen (Dinges & Powell, 1985; Lim & Dinges, 2008) (see Appendix A). Additionally, they were told to respond as quickly as possible when perceiving the appearance of a red and bright millisecond counter, which rapidly increased from zero, inside the rectangle. The millisecond counter appeared at random inter-stimulus intervals (ISI), which is the time period between the last response and stimulus appearance, ranging from 2 to 10 s (Lim & Dinges, 2008). The task was to tap the dominant hand's thumb on the screen as quickly as possible when the number was shown. Tapping the screen allowed the participant to view their reaction time, which was displayed in red for approximately 1 second. Then, the software proceeded to the next trial. If the participant used their non-dominant hand's thumb to respond, the software showed the error message *ERR.* If the participant tapped the screen before a number appeared, the error message *FS* (False Start) appeared. The participant was instructed to avoid these two errors. If the participant did not make a response within 60 s, the clock reset and counter restarted. When the task was completed, the participant was asked to indicate whether there were any distractors present during task performance by tapping numbers on a scale from "1" to "4+". The distractor indications alone were not used as a means to exclude participants. Based on subjective report, some participants indicated being distracted by intrusive thoughts and not by external distractions, and therefore indicated more distractions on the PVT. We only took into account participants' verbal indications of external distractions and distractions observed by the researcher when excluding PVT data. The duration of the experiment trial was 5 min and the participant completed a practice session before completing the experiment trials.

MST

The MST was used to assess pattern separation (Stark et al., 2013; Stark et al., 2019; Kirwan and Stark, 2007; Bakker et al., 2008; Toner et al., 2009; Ally et al., 2013; Bennett and Stark, 2016; Yassa et al., 2010b, 2011b). We used the MST version 0.97, set 1, and the task was presented on a desktop (Dell U2419H, Intel(R) Core(TM) i5-10505 CPU at 3.20GHz) or a laptop (Dell Inspiron 5559, Intel(R) Core (™) i5-6200U CPU at 2.30GHz). The pace of the task was computerized (i.e., not self-paced). The desktop had a 1920 x 1080 mm screen, whereas the laptop had a 1366 x 768 mm screen. Both computers' keyboards were positioned 20 cm away from the table edge. All sessions of the test were presented with Windows 10 across the two experimental conditions.

Task instructions were provided orally by the researchers using a script for phase 1 and phase 2 of the task (see Appendix A). The first session of the task (i.e., phase 1) had 128 trials. In each trial, participants were sequentially presented with images of everyday objects or items (i.e., targets) and asked to indicate via keyboard responses whether the object was an indoor or outdoor object (Stark et al., 2019; Stark et al., 2013). The participants were not informed about the upcoming memory test while they performed phase 1 of the task, which reduces the probability of mnemonic strategies such as active rehearsal of the images (Stark et al., 2013). During phase 2, which included 192 trials, the participants were sequentially presented with images of everyday objects again. This time, participants were asked to respond "old", "similar", or "new" to indicate whether the objects were a) identical to an image shown in phase 1 (i.e., target), b) similar to an image presented in phase 1 (i.e., lure, which varied in similarity), or c) a new photo not presented in phase 1 (i.e., foil) via keyboard presses. In the memory test phase (i.e., phase 2), one-third (64) of the images were identical to images shown in phase 1 (targets), one-third (64) of the images were perceptually similar to images seen during phase 1 (lures), and one-third (64) of the images were new (foils). All images in both phases were presented with a duration of 2000 ms with an inter-stimulus interval of 500 ms. The order of the presented images was counterbalanced between participants. The total duration of the task was 15 min.

REC is calculated as the difference between the probability of indicating "old" to repeated images (i.e., images that were included in phase 1) minus the probability of

indicating “old” to foils (hits minus false alarms) (Stark et al., 2013; Klippenstein et al., 2020). The LDI, on the other hand, is calculated as the difference between the probability of indicating “similar” to lure images minus the probability of indicating “similar” to foils (Stark et al., 2013, 2019). In addition, the lures included in the task varied in their extent of mnemonic similarity to repeated images, ranging from strong similarity (lure bin 1, or L1) to very low similarity (lure bin 5, or L5).

CANTAB

We used the *Prodromal Alzheimer’s disease and MCI CANTAB* battery to evaluate cognitive abilities that have shown sensitivity to normal cognition and aging as well as pre-clinical stages of Alzheimer’s disease (https://www.cambridgecognition.com/cantab/test-batteries/alzheimers-disease/). The battery included the following assessments and were administered in the following order: *Delayed Matching to Sample (DMS), Motor Screening Task (MOT), Paired Associates Learning (PAL), Reaction Time (RTI), and Spatial Working Memory (SWM)*. All tests were presented on an iPad (OS 15.4.1, model A2602, with a 260.6 x 174.1 mm screen size. The iPad was placed 20 cm away from the table edge in a horizontal position.

DMS

The Delayed Matching to Sample (DMS) test measured both simultaneous visual matching ability and short-term visual recognition memory, for non-verbalizable patterns. In addition, the task may also target pattern separation performance as it includes an interference component (Cambridge Cognition, 2021). During the task, the participant was shown a complex visual pattern that was both non-verbal and abstract (the sample) inside a red box for 4.5 s, and differed between each trial in terms of configuration and colour. Below this box, there were four white boxes, each containing different stimuli (choice stimuli); three containing a different pattern from the sample, and one containing a pattern identical to the sample. In the boxes with the patterns that differed, one box contained a pattern that had minimal or no overlap with the sample, and two boxes contained a pattern that differed from the sample in terms of position or colour. To discourage mnemonic strategies such as rehearsing the colour and shape of a single part of the shape, each of the 4 choice patterns had one randomly chosen quadrant in common. In some trials, the choice patterns and the sample appeared simultaneously, whereas in other trials, there was a delay of 0, 4, or 12 s before the four choices were

presented (Cambridge Cognition, 2021). Participants were given 4 practice trials, and each trial included one of the 4 conditions (i.e., simultaneous, 0 s delay, 4 s delay, or 12 s delay). The experiment trials included 5 trials of each condition and the conditions were presented in a random order. The participant was asked to select the pattern which exactly matched the sample. Participants were given auditory and visual feedback for incorrect or correct responses (red crosses or green ticks that were superimposed on the choice stimuli in addition to auditory tones). If the response was incorrect, the participant was allowed to choose again until selecting the correct stimuli. The outcome measures were latency (measured in milliseconds), the number of correct patterns selected, and a statistical measure providing the likelihood (%) of an error following an incorrect or correct response. Errors in each of the four test conditions (i.e., simultaneous, 0 sec delay, 4 sec delay, and 12 sec delay) were assessed to determine which of the three types of distractors (i.e., colour, shape, or unrelated) had been incorrectly selected. In each of the four conditions, the software computed mean RTs (i.e., latency before selecting stimuli) for trials in which the first choice had been correctly selected. The duration of the task was 7 min.

MOT

The Motor Screening task (MOT) provided a general assessment of whether reduced comprehension or impaired sensorimotor skills may lead to invalid participant data. During the task, colored (green and pink) crosses appeared in different screen locations and were presented one at a time. The participant was asked to touch the presented cross as accurately and quickly as possible. The task assessed the pointing accuracy (clicking the cross) and response speed of the participant. The duration of the Motor Screening Task was 2 min in total, but if participants understood the task and performed it correctly, the duration was approximately 18-22 s and about 10 trials were presented. If the participant did not perform the task correctly, the crosses stayed blinking in green and pink on the screen until the participant made the correct touch. Participants completed a practice session before the assessments.

PAL

The Paired Associates Learning (PAL) task provided a measurement of new learning and visual episodic memory. During the task, boxes were shown on the screen and were opened in a randomized order for 2 s. A pattern was located in one or more of

the boxes and no pattern was used for more than one set. The patterns were then presented in the center of the screen, one at a time. The participant was asked to select the box in which the pattern was originally displayed. The boxes were opened in sequence again to remind the participants of where the patterns were located if an error was made. The first level included 6 boxes and two stimuli locations to remember. The task became gradually more challenging. The next levels included 4 locations to remember, then 6 locations, and finally 8 locations. The final level also included 8 boxes for the 8 locations. The difficulty levels ensured that participants understood the basic requirements of the task and that the task challenged each participant's visual memory capacity. The participant had up to 3 attempts in each level to complete the level. If one or more choices were incorrect, the boxes were successively reopened randomly for 2 s each. If the participant made one or more errors in the third attempt before the end of the total duration of 8 min, the software terminated the PAL automatically and proceeded to the next test. The task's outcome measures were the participant's errors, the number of trials required to accurately locate the patterns, memory scores, and number of completed levels. The participant also completed a practice session before the assessment.

5-Choice RTI

The 5-Choice Reaction Time Inventory (RTI) task assessed movement time (i.e., rate at which one responds to a stimulus), in addition to reaction time (i.e., the time it takes to respond to a stimulus), response accuracy, and divided attention. During the task, the participant was asked to select and hold a button at the bottom of the screen. The participant was asked to press down a button at the bottom of the screen to make a yellow flash appear in one of five circles presented at the top of the screen. Once the flash appeared, the participant was instructed to react as quickly as possible by releasing the button at the bottom of the screen and touching the circle in which the yellow flash appeared. The outcome measures were divided into movement time and reaction time. The duration of the Reaction Time Task was 3 minutes and participants completed 9 practice trials before the assessment.

SWM

The Spatial Working Memory (SWM) task required manipulation and retention of visuospatial information. During this task, a number of colored boxes were presented on

the screen and could be opened by touching the screen. When selecting the boxes, the participant could find one yellow token in each of a number of boxes. The participant was asked to select the boxes by using an elimination process in which possible choices or boxes were selected one by one until the target was located or only one box remained containing the target. Only one token was hidden at a time. The tokens that were found filled up an empty column on the right side of the screen. The targets were hidden no more than once in the same box and the participant was instructed to click on the boxes only once. The test included 4 difficulty levels. The first level included 4 purple boxes. The next level included 6 orange boxes, and the final level included 8 blue boxes. The participants also completed 2 practice trials including 3 boxes in each trial. In order to discourage stereotyped search strategies, the position and color of the boxes varied from trial to trial. This self-ordered test assessed executive functions and measured working memory errors. Outcome measures included search strategy and errors. The errors included selecting boxes that had already been identified as empty or reselecting boxes that already had been found to include a token (Naëgelé et al., 2006). The duration of the task was 4 minutes.

2.4. Data analysis

The effects of sleep on cognitive performance were assessed using two-tailed Pearson's correlational analyses run in the software Prism Graphpad 9.0 (GraphPad Software, Boston, USA). Two-tailed statistical tests were used and results were considered statistically significant when $p < 0.05$. Specifically, we ran correlations between total sleep time, sleep onset latency, sleep efficiency, and WASO, and the PVT, MST, and CANTAB outcome measures. Because of the exploratory nature of this study, we did not control for multiple comparisons. Correlations that violated the assumption of normality were conducted using Spearman's rank correlation (ρ).

2.4.1. Actigraphy

Actigraphy data were analyzed with ActStudio (Condor Instruments, 2022), version 1.0.23. Only nocturnal sleep was assessed. To analyze actigraphy data, we used light, temperature and activity levels as indicators of sleep and wakefulness. Additionally, we used event button presses as indicators of bedtime and get-up time. To

record bedtime and get-up time, sleep diary marks were inserted where the participant appeared to go to bed (e.g., light and activity levels decreased, and event button pressed) and get-up (e.g., visible spikes in light and activity levels, and event button pressed). The sleep parameters generated by the ActStudio Software were the overall means and standard deviations (i.e., across the week) for the following measures: 1) sleep onset latency, which is defined as the time period between going to bed and sleep onset; 2) total sleep time, which is the amount of time (in hours and minutes) between sleep onset and sleep end; 3) sleep efficiency, which is defined as the ratio of total time spent asleep compared to total time in bed, provided as percentage; 4) wake after sleep onset (WASO), which is the total number of minutes that a person is awake after having initially fallen asleep; 5) total number of nocturnal awakenings, which is the number of times the participant woke up throughout the night. We chose to focus on only 4 specific sleep parameters to represent sleep amount and sleep quality in our analyses; total sleep time, sleep onset latency, sleep efficiency, and WASO. A minimum of 5 nights of good quality actigraphy data was required for each participant to be included in the analysis. Our data were sampled in 1-min epochs (i.e., 60 seconds interval) (Cole & Kripke, 1992).

2.4.2. Sleep diary

Sleep diary data aided actigraphy analysis by confirming bed and wake times, and for assisting analysis when actigraphy data were obscure. Participants did not have to complete diaries for all 7 days to be included in the analysis (Mallinson et al., 2019).

2.4.3. NASA-PVT

The performance metrics calculated for the 5-minute simple PVT from NASA included 1) mean 1/RT, which is the average reciprocal response speed (measured in seconds); 2) the total number of lapses, which is the number of times the reaction times exceeded 500 ms; 3) optimum response domain, which is the average of the fastest 10% reaction times for all trials indicating the highest performance a participant is capable of producing; 4) mean slowest 10% reaction times, which is the average of the 10% slowest reaction times for all trials; 5) cognitive slowing, which is the slowest 10% of reciprocal response times for all trials indicating the vigilance response slowing (i.e., slowest 10% 1/RT, measured in seconds). These measures were used in previous

studies evaluating sleep and PVT metrics and have been shown to be most sensitive to sleep loss (Basner & Dinges, 2011; Loh et al., 2004; Arsintescu et al., 2017; Thompson et al., 2022). For mean 1/RT and cognitive slowing, a reciprocal transformation was applied to the raw data in accordance with Dinges & Kribbs' (1991) methodology. This procedure reduces the influence of long lapses and emphasizes response slowing in intermediate and optimum ranges (Dinges et al., 1991).

2.4.4. MST

The Memory Recognition scores (REC) for old (i.e., repeat) images were calculated by subtracting the rate of "old" responses provided to foils from the rate of "old" responses provided to old, or repeated, images [p (correct old response to lures) - p (false old response to foils)] (Stark et al., 2013), where "p" stands for probability. This analysis procedure assesses recognition memory and corrects for any response bias. The Lure Discrimination Index (LDI) was calculated by subtracting the probability value of "Similar" responses provided to the foils from the probability value of "Similar" responses provided to the lures [p (correct similar response to lures) - p (false similar response to foils)] (Stark et al., 2013). This was done in order to correct for any response biases toward the tendency of continuously using the "Similar" response in addition to calculating pattern separation scores. Additionally, the LDI was calculated for each of the separate lure bins, using the same incorrect "similar" response to foils used for the overall LDI analysis.

2.4.5. CANTAB

The prodromal AD and MCI battery included the Delayed Matching to Sample (DMS), Motor Screening Task (MOT), Paired Associates Learning (PAL), Reaction Time (RTI), and the spatial Working Memory (SWM).

DMS

The sub-measures we were most interested in included 1) *DMS Mean Correct Latency (DMSML):* The mean latency between the presentation of the response stimuli options and the subject selecting the correct box on their first attempt. Calculated across all correct assessed trials (simultaneous and all delays); 2) *DMS Mean Correct Latency (0 seconds delay) (DMSML0)*: The mean latency between the presentation of the

response stimuli options and the subject selecting the correct box on their first attempt for trials containing a zero second delay. Calculated across all assessed trials containing a zero second delay; 3) *DMS Mean Correct Latency (4 seconds delay) (DMSML4):* The mean latency between the presentation of the response stimuli options and the subject selecting the correct box on their first attempt for trials containing a four second delay. Calculated across all assessed trials containing a four second delay; 4) *DMS Mean Correct Latency (12 seconds delay) (DMSML12):* The mean latency between the presentation of the response stimuli options and the subject selecting the correct box on their first attempt for trials containing a twelve second delay. Calculated across all assessed trials containing a twelve second delay; 5) *DMS Mean Correct Latency (All Delays) (DMSMLAD):* The mean latency between the presentation of the response stimuli options and the subject selecting the correct box on their first attempt for trials containing a delay between target and response stimuli presentation. Calculated across all assessed trials containing a delay (0 s, 4 s, or 12 s); 6) *DMS Mean Correct Latency Simultaneous (DMSMLS):* The mean latency between the presentation of the response stimuli options and the subject selecting the correct box on their first attempt for trials containing a simultaneous presentation of target and response stimuli. Calculated across all assessed trials containing simultaneous presentation.

MOT

We used the sub-measure 1) The total number of assessment trials on which the subject failed to make a correct response (MOTTE). The motor task was included to assess participants' general sensorimotor performance and task comprehension in order to ensure that participant data collected during CANTAB testing were valid.

PAL

The sub-measures we were most interested in included 1) *PAL First Attempt Memory Score (PALFAMS):* The number of times a subject chose the correct box on their first attempt when recalling the pattern locations. Calculated across all assessed trials; 2) *PAL Mean Errors to Success (PALMETS):* The mean number of attempts made by a subject needed for them to successfully complete the stage; 3) *PAL Total Errors (Adjusted) (PALTEA):* The number of times the subject chose the incorrect box for a stimulus on assessment problems, plus an adjustment for the estimated number of errors they would have made on any problems, attempts and recalls they did not reach.

This measure allows you to compare performance on errors made across all subjects regardless of those who terminated early versus those completing the final stage of the task; 4) *PAL Total Errors 2 Shapes (Adjusted) (PALTEA2):* The number of times the subject chose the incorrect box for a stimulus on assessment problems, where the number of shapes required to remember was equal to 2, plus an adjustment for the estimated number of errors they would have made on any other 2 pattern problems, attempts and recalls they did not reach, 5) *PAL Total Errors 4 Shapes (Adjusted) (PALTEA4):* The number of times the subject chose the incorrect box for a stimulus on assessment problems, where the number of shapes was equal to 4, plus an adjustment for the estimated number of errors they would have made on any other 4 pattern problems, attempts and recalls they did not reach, 6) *PAL Total Errors 6 Shapes (Adjusted) (PALTEA6):* The number of times the subject chose the incorrect box for a stimulus on assessment problems, where the number of shapes was equal to 6, plus an adjustment for the estimated number of errors they would have made on any other 6 pattern problems, attempts and recalls they did not reach, 7) *PAL Total Errors 8 Shapes (Adjusted) (PALTEA8):* The number of times the subject chose the incorrect box for a stimulus on assessment problems, where the number of shapes was equal to 8, plus an adjustment for the estimated number of errors they would have made on any other 8 pattern problems, attempts and recalls they did not reach.

5-Choice RTI

We included the sub-measure *RTI Mean Five-Choice Movement Time (RTIFMMT):* The mean time taken for a subject to select the target stimulus after releasing the response button. This measure is calculated across all correct, assessed trials in which the stimulus could appear in any of the five locations. It was measured in milliseconds.

SWM

*W*e included the sub-measures 1) *SWM Between Errors (SWMBE, key measure)*: The number of times the subject incorrectly revisited a box in which a token had previously been found. Calculated across all assessed four, six and eight token trials; 2) *SWM Between Errors 4 boxes (SWMBE4, key measure)*: The number of times a subject revisited a box in which a token had previously been found. Calculated across all trials with 4 tokens only; 3) *SWM Between Errors 6 boxes (SWMBE6, key measure):* The

number of times the subject revisited a box in which a token had previously been found. Calculated across all trials with 6 tokens only; 4) *SWM Between Errors 8 boxes (SWMBE8, key measure):* The number of times the subject revisited a box in which a token had previously been found. Calculated across all trials with 8 tokens only; 5) *SWM Strategy (6-8 boxes) (SWMS, key measure):* The number of times a subject began a new search pattern from the same box they started with previously. If they always begin a search from the same starting point, we infer that the subject is employing a planned strategy for finding the tokens. Therefore, a low score indicates high strategy use (1 = they always begin the search from the same box), and a high score indicates that they are beginning their searches from many different boxes. Calculated across assessed trials with 6 tokens or more.

2.4.6. MoCA

The MoCA has 11 categories of scores (Alternating Trailmaking, Visuoconstructional Skills including cube, Visuoconstructional Skills including clock, Naming, Memory, Attention, Sentence Repetition, Verbal Fluency, Abstraction, Delayed Recall, and Orientation) that sum to a total of 30. In addition to assessing MoCA scores in relation to sleep assessments, we also ran Pearson correlations between the older adults' MoCA scores and CANTAB's DMS, RTI, PAL, and SWM sub-measures specified above.

2.4.7. Clocklab

Clocklab is a widely used stand-alone software to assess circadian rhythms and other chronobiology measures (Actimetrics, Wilmette, USA). It provides tools for recording, processing, and interpreting circadian rhythm data. For the Clocklab analysis, we used Clocklab version 6.1.11. We focused on the acrophase; the time of the peak of a circadian rhythm through a fitted cosine wave, in addition to non-parametric circadian rhythm parameters including amplitude; the strength or magnitude of a circadian rhythm over a 24 h period, interdaily stability (IS); the stability and consistency of a circadian rhythm across multiple days, and intradaily variability (IV); the circadian variability or fluctuations that occur within a 24-hour circadian cycle. We ran correlations between these parameters and the MST and CANTAB sub-measures.

2.4.8. Independent t-tests

We also ran independent t-tests. The normality assumption was assessed using the Shapiro-Wilk's test. Normal data are presented as mean ± SEM. For data that violated the normality assumption, we ran the Mann-Whitney U test and reported data as median (MD) and interquartile range (IQR). For effect sizes of statistically significant tests, Cohen's D is reported for independent t-tests, and rank-biserial correlation (r_{rb}) is reported for Mann - Whitney U tests. We chose to use independent t-tests instead of Analysis of Variance (ANOVA) as we wanted to obtain a direct comparison between the different groups. We also did not intend to examine interactions between two or more factors. Moreover, the t-tests were post-hoc tests and we did not have the power to assess interactions effectively. Conducting the independent t-tests, we compared older and younger adults' sleep (i.e., total sleep time, sleep onset latency, sleep efficiency, and WASO) and performance on the cognitive tests. In addition, we compared males and females in both groups on the different sleep measures and cognitive measures. Last, we compared good sleepers versus bad sleepers on the different cognitive tests. Actigraphy data was used for this analysis, and we examined sleep efficiency and total sleep time by separating the 25% highest and 25% lowest scores. A Bonferroni correction was applied for analyses for sleep and cognitive measures to correct for multiple comparisons. Using 5 different outcome variables for the PVT, a $p = .01$ was considered significant, using 7 outcome variables for MST yielded a significance value of $p = .007$, and for CANTAB with 19 outcome measures, the significance value was $p = .003$.

2.5. Results

2.5.1. Sample characteristics

A total of 9 students were excluded from all analyses due to unreliable or missing actigraphy data (no actigraphy data recorded or the participant removed the actigraphy watch during sleep period), and one participant was older than 30 years of age, leaving 79 participants (age range: 18 - 30 years, mean age: 20.10 ± 1.93, 48 females) included in one or more of the cognitive analyses. All participants identified themselves as female or male. Three students were excluded from PVT analyses due to major distractions (reported by participant and observed by the researcher) during task performance, 10

students were excluded from MST analyses due to response bias or a REC score below the cutoff value of 50%, and 6 students were excluded from CANTAB due to missing data, CANTAB malfunctioning or being unable to concentrate.

A total of 6 older adults were excluded from all analyses. Three participants were excluded from all analyses due to not following task instructions or misunderstanding the tasks, 2 participants were excluded due to not having valid data on both CANTAB and MST, and 1 participant did not comply with watch wearing at night, leaving 34 participants (age range: 51 - 84, mean age: 65.76 ± 9.76, 18 females) included the analyses. Five participants were excluded from PVT analyses due to failing to press the iPad screen or pressing when not intending to do so, and to verbally reporting being distracted by noise. Twelve participants were excluded from MST analyses due to using the wrong keyboard keys, and no participants were excluded from CANTAB. All participants' demographic information are displayed in Table B.1 in Appendix B.

2.5.2. Sleep

Actigraphy

Mean ± SD for the different sleep parameters for the younger and older adults are presented in Table B.2 in Appendix B.

Sleep diary

The sleep diaries were used to confirm actigraphy bed and waketimes. The older adults provided more detailed sleep diaries compared to the younger adults. Both groups showed similar level of compliance in completing the diary across the 7 days, where 89.87% (71/79) of the younger participants and 91.18% (31/34) of the older participants completed all 7 entries. The lowest number of entries among the younger participants was 4 (1 participant), and the lowest number of entries among the older participants was 6 (3 participants).

2.5.3. Pearson's correlations

NASA-PVT

Table B.3 (see Appendix B) displays correlations between the sleep parameters and the 5 PVT metrics for the younger and older adult data. There was a significant correlation between 10% slowest RT and total sleep time (r = -.39, p = .04) and sleep efficiency (r = -.43, p = .02) (Fig. 2.1), and between cognitive slowing and sleep efficiency (r = .39, p = .04) in the older adult PVT data. Correlations between cognitive slowing and total sleep time (r =.36, p= .06*)* and between 10% slowest RT and WASO (r = .36, p = .053) in the older adult data almost reached significance. In the younger adult data, the correlation between WASO and 10% slowest RT (ρ = .24, p = .04) and cognitive slowing (ρ = -.24, p = .04) (Fig. 2.1) were significant. In addition, the correlations between sleep efficiency and 10% slowest RT (ρ = -.20, p = .08) and cognitive slowing (ρ = .22, p = .06) were close to a significant result.

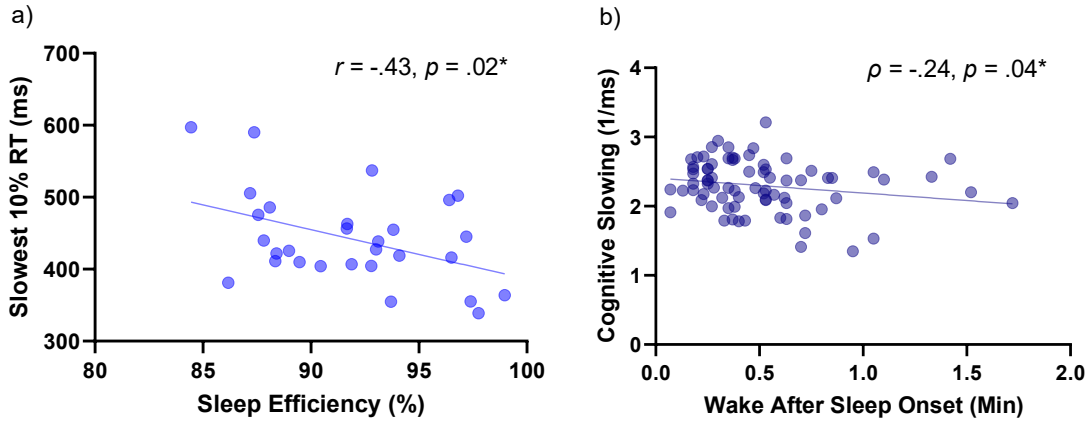

Figure 2.1. a) Pearson's correlation between 10% slowest RT and sleep efficiency in the older adults b) Spearman's correlation between cognitive slowing and WASO in the younger adults.

MST

Table B.4 (see Appendix B) displays correlations between the MST measures and the 4 actigraphy sleep parameters for the younger and older adult data. In the younger and older adult data, there were no significant correlations between the LDI and the sleep parameters. The correlations between REC and the sleep parameters did not reach statistical significance. In the younger adult data, the correlation between lure bin 5 and WASO almost reached significance (ρ = -.22, p = .052) (Fig. 2.2). There were no significant correlations between the other 4 lure bins and the sleep parameters. In the

older adult data, the correlation between lure bin 1 and total sleep time (r = .40, p = .06) was close to significance, and graphical display of the correlation does indicate a non-significant relationship (Fig. 2.2). No other results were close to statistical significance.

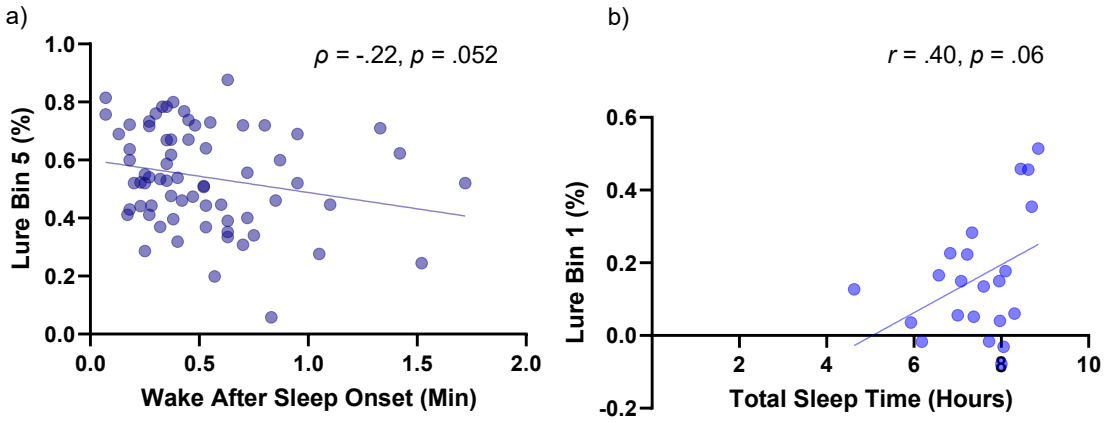

Figure 2.2. a) Spearman's correlation between L5 and WASO in the younger adults b) Pearson's correlation between L1 and total sleep time in the older adults.

CANTAB

Table B.5 (see Appendix B) displays correlations between the CANTAB measures DMS, PAL, RTI, and SWM, and the 4 actigraphy sleep parameters for the younger and older adults. All participants committed 0% errors on the MOT. As the MOT provides a general assessment of whether sensorimotor deficits will limit collection of valid participant data, this result indicates that all participants were able to interact with the task components.

DMS

We did not observe any significant relationships between the sleep parameters and the DMS measures. In the younger adult data, the correlation between sleep efficiency and DMSML12 (ρ = .18, p = .13) does show a non- significant relationship that is affected by outliers (Fig. 2.3). In the older adult data, there was a significant correlation between DMSML4 and sleep efficiency (r = -.37, p = .03) (Fig. 2.3) and between DMSML4 and WASO (r = .39, p= .02). No other correlations reached statistical significance.

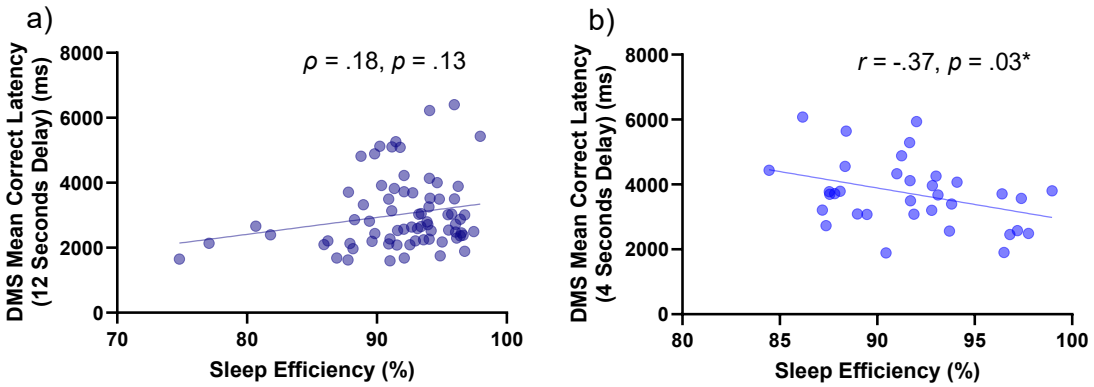

Figure 2.3. a) Spearman's correlation between DMSML12 and sleep efficiency in the younger adults b) Pearson's correlation between DMSML4 and sleep efficiency in the older adults.

PAL

In the younger adult data, none of the correlations between the PAL sub-measures and the sleep parameters were statistically significant (Table B.5 in Appendix B). In the older adult data, no correlations reached statistical significance (Table B.5 in Appendix B). However, the correlation between PALTEA2 and WASO (ρ = .31, p = .07) and between PALTEA6 and sleep onset latency (ρ = -.30, p = .09) was close to a significant result.

5-Choice RTI

There were no significant correlations in the older adult data. In the younger adult data, the correlation between RTIFMMT and sleep onset latency was almost significant (ρ = -.21, p = .07).

SWM

As shown by Table B.5, there was a significant correlation between SWMBE6 and sleep efficiency (ρ = -.24, p = .04) and a significant correlation between SWMBE6 and WASO (ρ = .27, p = .02) in the younger adult data. There were no significant correlations between the SWM sub-measures and the sleep parameters in the older adult data.

MoCA

We performed Pearson's correlations to assess the relationship between the sleep parameters and the total MoCA score. Results revealed non-significant correlations between the MoCA and total sleep time (r = .10, p = .28), sleep onset latency (ρ = .22, p

= .21), sleep efficiency (r = .23, p = .18), and WASO (r = -.22, p = .21). We also assessed the relationships between the MoCA and the CANTAB measures described above. As shown by Table B.6 (Appendix B), most of the PAL and SWM sub-measures were significantly and negatively associated with the participants' MoCA score.

Clocklab

We focused on the acrophase, amplitude, IS, and IV. In the younger adult sample, there was a close to significant correlation between amplitude and LDI (ρ = .28, p =.06) (Fig. 2.4), and a significant correlation between amplitude and lure bin 2 (ρ = .36, p = .02) (Fig. 2.4), and lure bin 4 (ρ = .35, p =.02) (Fig. 2.4). There was also a significant negative correlation between IV and lure bin 4 (r = -.41, p = .01) (Fig. 2.4). In the older adult sample, the results revealed a significant correlation between IV and LDI (r = .56, p = .01) (Fig. 2.5), lure bin 1 (r = .48, p = .03) (Fig. 2.5), lure bin 2 (r = .46, p =.04) (Fig. 2.5), lure bin 3 (r = .53, p = .01) (Fig. 2.5), lure bin 4 (r =.56, p = .01) (Fig. 2.5), and lure bin 5 (r = .61, p =.003) (Fig. 2.5). The remaining results are displayed in Table B.7 in Appendix B.

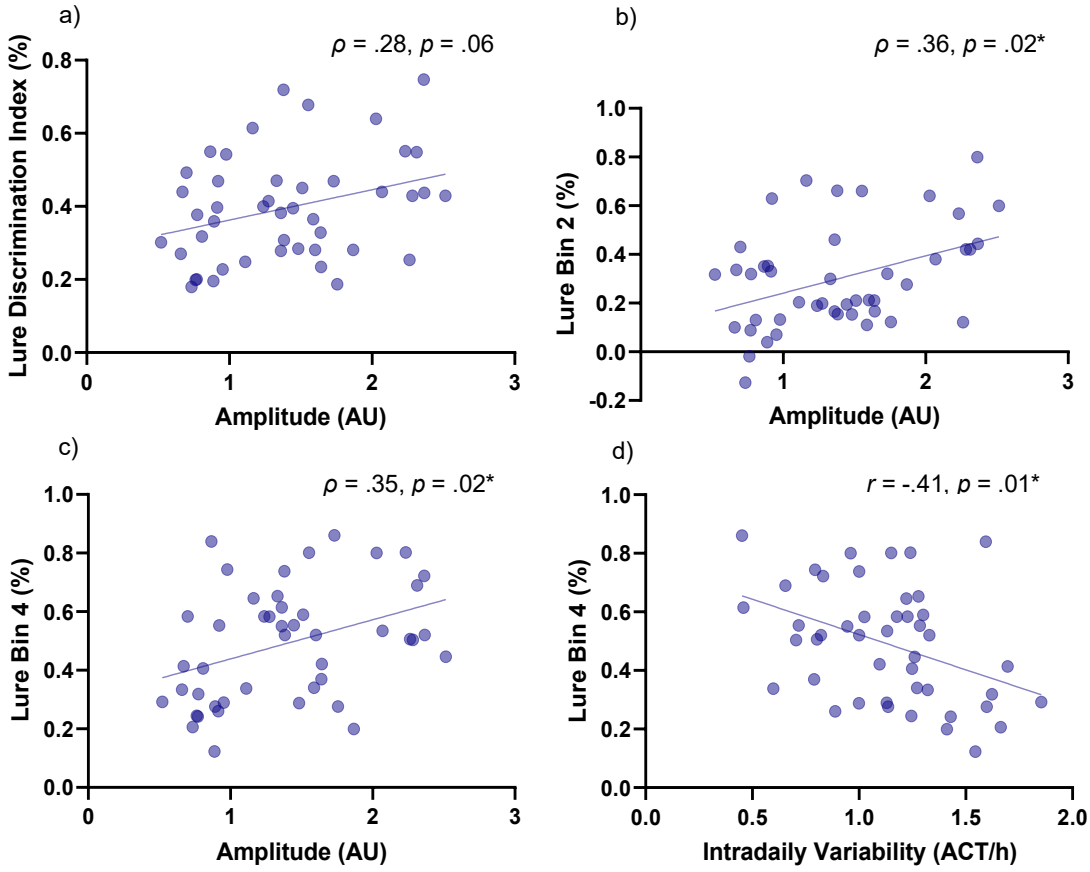

Figure 2.4. **Graphs are displaying the younger adults' performance on the MST. a) Spearman's correlation between LDI and amplitude b) Spearman's correlation between L2 and amplitude c) Spearman's correlation between L4 and amplitude d) Pearson's correlation between L4 and IV.**

Note. On the x-axis, AU indicates *arbitrary units* and ACT/h indicates *activity counts per hour.*

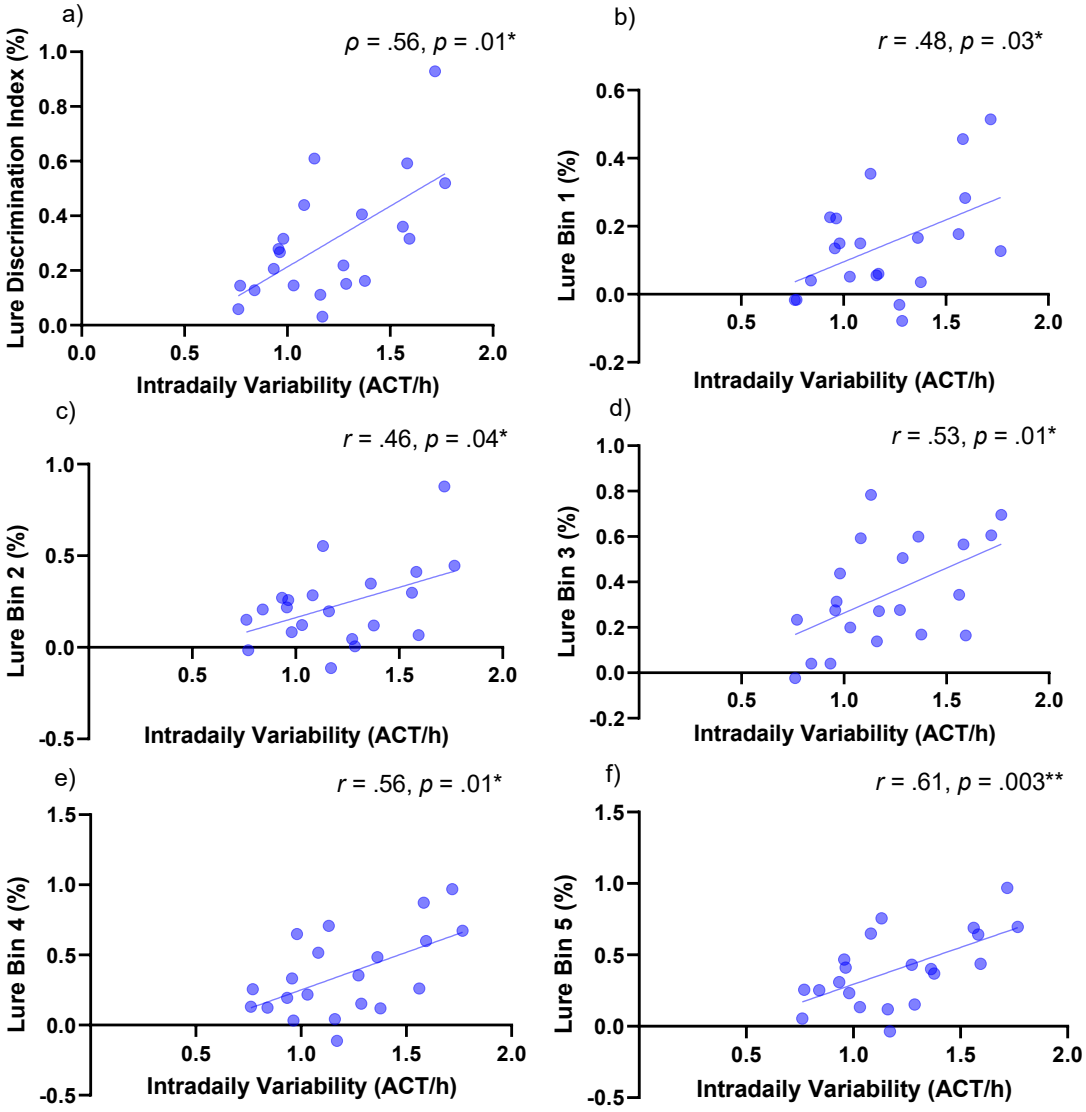

Figure 2.5. **Graphs are displaying the older adults' performance on the MST. a) Spearman's correlation between LDI and IV b) Pearson's correlation between L1 and IV c) Pearson's correlation between L2 and IV d) Pearson's correlation between L3 and IV e) Pearson's correlation between L4 and IV f) Pearson's correlation between L5 and IV.**

Note. On the x-axis, ACT/h indicates *activity counts per hour.*

In the younger adult CANTAB data, there was a significant correlation between acrophase and DMSML0 (ρ = .32, p = .03). The correlation between acrophase and DMSMLAD was also close to a significant result (ρ = .27, p = .08). In the older adult CANTAB data, there was a significant correlation between acrophase and SWMBE4 (ρ = .37, p = .04). The remaining results are displayed in Table B.8 in Appendix B.

2.5.4. Independent t-tests

The younger and older participants were compared on sleep parameters including total sleep time, sleep efficiency, WASO, and sleep onset latency. We also compared the older and younger adults on the cognitive measures described above including PVT, MST, and CANTAB. Last, we compared the sexes within each group in addition to good and bad sleepers.

Sleep

There were no significant differences between younger (MD = 7.00, IQR = .03 - .08) and older (MD = 7.00, IQR= .03 - .08) adults' sleep onset latency (U = 1324, p = .90), between younger (MD = 92.54, IQR = 89.83 - 94.88) and older (MD = 91.70, IQR = 88.29 - 93.89) adults sleep efficiency (U = 1240, p = .42), and between younger (MD = .42, IQR = .27 - .63) and older (MD= .55, IQR = .37 - .81) participants' WASO (U = 1122, p = .17). However, there was a significant difference between younger and older adults' total sleep time [t(111)= 3.26, p = .001] in that younger adults had a shorter total sleep time compared to the older adults (Fig. 2.6). In the younger adults, sex differences revealed that females (6.93 ± .11) compared to males (6.47 ± .15) had a non-significantly longer total sleep time [t(77)= 2.45, p = .02]. Sex differences in sleep in both samples are displayed in Table B.9 and B.10 in Appendix B.

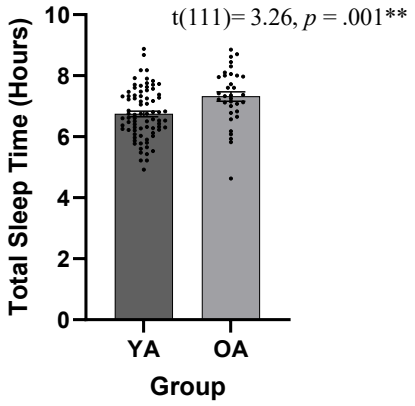

Figure 2.6. Bar graph comparing younger and older adults' total sleep time.

MST

A Mann-Whitney U test revealed a significant difference between the older and younger adults on LDI performance (U = 471, p = .007) (Fig. 2.7). In addition, independent t-tests with Welch correction showed non-significant differences between the younger and older adults' performance on lure bin 4 [t(27.05) = 2.47, p = .02] (Fig. 2.7) and lure bin 5 [t(27.28) = 2.55, p = .02] (Fig. 2.7). Across the tests, the younger adults performed better than the older adults, but most findings were non-significant. Results are displayed in Table B.11 in Appendix B.

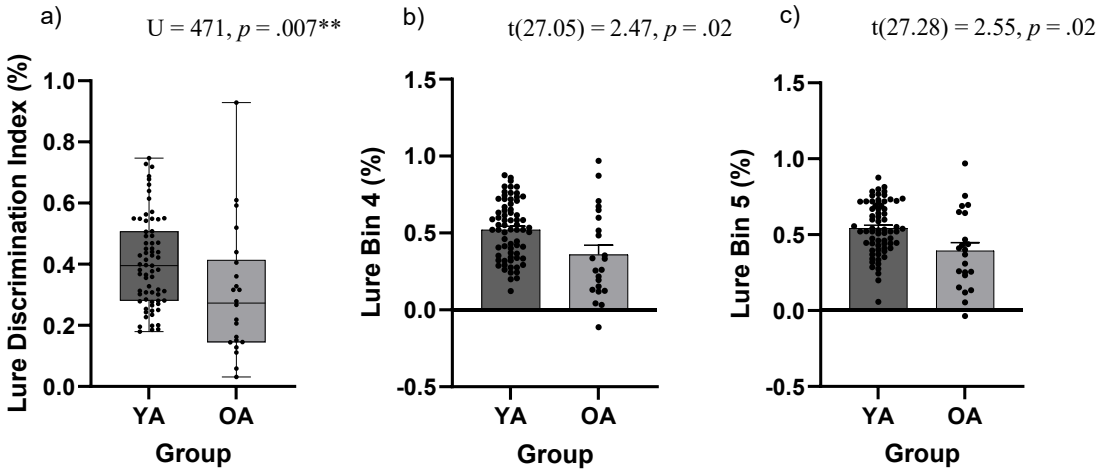

Figure 2.7. a) Boxplot comparing younger and older adults' LDI performance b) Bar graph comparing younger and older adults' L4 performance c) Bar graph comparing younger and older adults' L5 performance.

CANTAB

The younger and older adults were compared on the different CANTAB measures and the results are displayed in Table B.12 in Appendix B. As shown in the table, almost all of the Mann-Whitney U tests showed significance with Bonferroni correction. The Mann-Whitney U test between younger and older adults' performance on PALTEA2 did not reach statistical significance (U=1132, p = .03) with Bonferroni correction.

Sex analyses

We performed independent t-tests to compare females' and males' cognitive performance on the MST and CANTAB in the younger and older participant samples. In the younger adult MST data, there were no differences between the sexes (p >.01) (see

Table B.13 in Appendix B). There were also no differences between the sexes in the older adult data (see Table B.14 in Appendix B). Next, we ran independent t-tests in the CANTAB data. In both the younger and older adult CANTAB data, there were no significant performance differences between the sexes (p >.003). Results are displayed in Table B.15 and B.16 in Appendix B.

Good versus bad sleepers

We performed independent t-tests to compare good and bad sleepers in the younger and older participants' CANTAB and MST performance. We focused on sleep efficiency and total sleep time for this analysis. We did not compare older adult good and bad sleepers on MST performance in terms of sleep efficiency due to low participant number in the bad sleeper group (N = 3). In the younger and older adult MST data, independent t-test revealed no significant differences between good sleepers and bad sleepers (p >.01). Results are displayed in Table B.17, B.18, and B.19 in Appendix B. Next, we ran independent t-tests between good and bad sleepers in the younger and older adult CANTAB performance. Results are displayed in Table B.20, B.21, B.22, and in B.23. Independent t-tests revealed no significant differences in the younger and older adult CANTAB performance between good and bad sleepers based on sleep efficiency and total sleep time. Graphical display showed that bad sleepers in terms of sleep efficiency in the younger adult data committed more errors on the SWMBE (Fig 2.8), SWMBE6 (Fig. 2.8), and SWMBE8 (Fig. 2.8), compared to good sleepers, but this was not statistically significant.

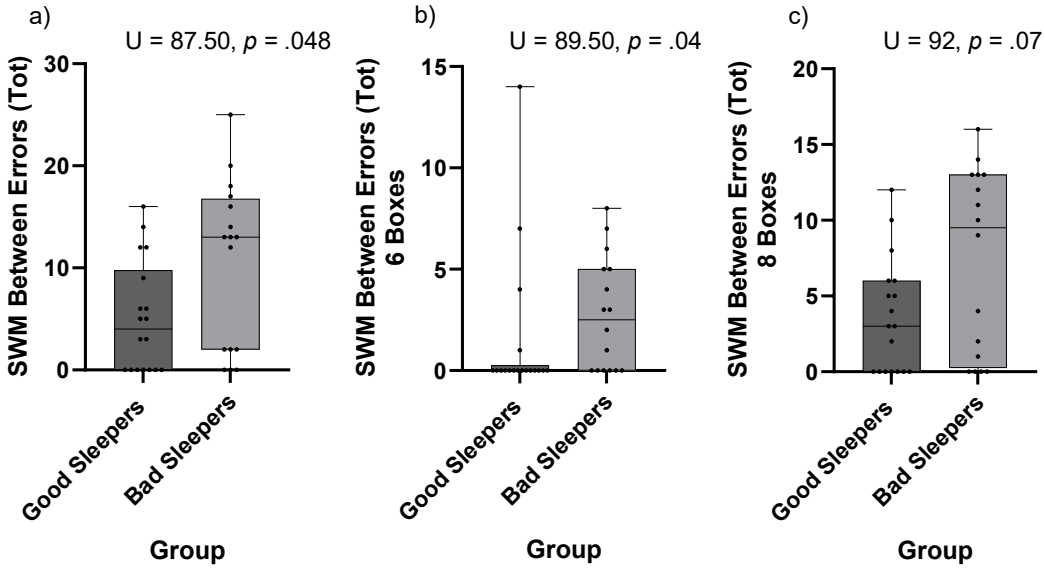

Figure 2.8. Graphs displaying younger adults' performance on CANTAB SWM. a) Boxplot comparing good and bad sleepers' performance on SWMBE b) Boxplot comparing good and bad sleepers' performance on SWMBE6 c) Boxplot comparing good and bad sleepers' performance on SWMBE8.

2.6. Summary

In this exploratory correlational study, we examined many different cognitive variables and how they are related to sleep quality and quantity. Across the different correlations, we can see that sleep seems to be associated with pattern separation performance in both the younger and older adults. Specifically, on the MST, sleep quantity (i.e., total sleep time) showed a relationship with the lure bin 1 in the older adult sample, and sleep quality (i.e., WASO) showed a relationship with lure bin 5 in the younger adult data. On the CANTAB, we observed relationships between sleep and the DMS sub-measures in both the younger and older adults. In the older adults, these sleep and CANTAB relationships appeared to be stronger. This might indicate that pattern separation is associated with sleep in both younger and older adults, and that particularly older adults' level of sleep quantity and quality affects pattern separation performance. In the other CANTAB measures (i.e., PAL, RTI, and SWM), we did see relationships between some of the sleep measures (i.e., sleep efficiency and WASO), although most of the relationships were weaker compared to the correlations between DMS and sleep. This suggests that the CANTAB DMS is most sensitive to sleep. We also observed some relationships between some of the circadian rhythm measures and cognitive performance (i.e., between amplitude and LDI, lure bin 2, and lure bin 4, and between IV and lure bin 4) in the younger adults. In the older adults, the positive and significant relationships between IV and the different MST measures are in conflict to what the literature says about cognitive performance (Rabinowitz et al., 2022). Across the independent t-tests between good and bad sleepers, we observed based on graphical and table display that those characterized as good sleepers generally performed non-significantly better compared to the bad sleepers. There were no sex differences in either group, however, there were differences in terms of age effects on cognitive performance. The younger adults overall showed superior performance compared to the older adults on the different cognitive tests (i.e., MST and CANTAB), which is to expect according to the literature.

Chapter 3.

An experiment on sleep deprivation and cognitive performance

In a second study, we examined the effects of 24 hours total sleep deprivation and a rested condition on cognitive performance in healthy young adults. To measure cognitive performance, we used the same cognitive measures as we used in the correlational study reported above. We aimed to examine whether total sleep deprivation would lead to impairment on the tests that were shown to be correlated with habitual sleep parameters above. We predicted that participants in the sleep deprivation condition would show poorer MST and CANTAB performance compared to the rested controls.

3.1. Methods

3.1.1. Research subjects

The study was approved by the Simon Fraser University's Research Ethics Board (REB) (protocol #30000687) and included a rested and a sleep deprivation condition. Subjects in the rested condition were 32 undergraduate students recruited via SFU's Sona/RPS system (sona-systems.com). Subjects in the sleep deprivation condition were 16 undergraduate and graduate students recruited via posters, lectures, word-of-mouth, and social media platforms. Prior to any testing, participants completed an online consent form and a Subject Information Survey. The participants' responses to the questions in the Subject Information Survey determined their eligibility to participate in the study. Exclusion criteria for participants in the rested condition were inability to provide proof of COVID-19 vaccination, visual disorders that could not be corrected with lenses, self-reported health concerns (e.g., sleep disorders, neurological disorders, and/or mental health issues), left-handedness, allergy to rubbing alcohol, and age greater than 40 or less than 18 years, stated in the consent form. Additional exclusion criteria included poor fluency in English, frequent use of psychoactive substances (e.g., marijuana), working night shifts, and having traveled across multiple time zones within the past month (i.e., trans-meridian flight). Exclusion criteria for participants in the sleep

deprivation condition were all of the above in addition to living off-campus or not having a safe ride home, and an inability to wear contact lenses if they were dependent on vision corrections. The subjects in the rested condition received 6 RPS credits upon completion or were paid $30, whereas the subjects in the sleep deprivation condition were compensated with $100.

3.1.2. Experimental protocol

An experimental between-group design was used, involving two conditions; a rested condition and a 24-hour total sleep deprivation (TSD) condition. On day 1, participants were scheduled to arrive in the laboratory for their first visit to complete a consent form and a sleep diary. Participants were also provided with an actigraphy watch. Following the first lab visit, participants went about their normal life and were asked to refrain from napping, drinking caffeinated drinks, and performing excessive exercises. Physical activity was monitored with actigraphy.

In the sleep deprivation condition, at 11 pm, participants returned to the lab to spend the night awake. The participants were provided with UVEX S1933X blue-wavelength-blocking glasses to limit phase-shifting effects caused by light exposure during the night. During the night of sleep deprivation, light snacks, such as bananas and chips, and non-caffeinated beverages were provided, and participants were also allowed to bring their own food. Napping and performing intense physical exercise were prohibited. Participants were permitted to walk around, read, watch movies, play board and computer games and listen to music. Two research assistants constantly monitored the participants ensuring that the participants wore the blue-wavelength-blocking glasses and stayed awake. The next morning (between 5 am and 7 am) participants completed another sleep diary. Thereafter, the participants could choose whether they wanted to stay in the lab or go home and then return for their cognitive test appointment, which was scheduled 24 hours after their first lab visit. Before their test appointment, participants handed back the actigraphy watch.

In the rested condition, participants were scheduled for two lab visits. All visits took place between 8:00 am and 3:00 pm, and participants were able to choose a timeslot that would work best for them to participate. During the first visit, participants completed a consent form, a sleep diary, and were provided with an actigraphy watch.

On the next visit, which took place 24 hours after the first visit and a full night of sleep, participants completed another sleep diary, handed back the actigraphy watch, and were assessed on a range of cognitive tests. A step-by-step study guide standardizing data collection, including scripts, instructions, set-up, and order of procedures, was followed by the experimenter during every test session. All participants also participated in a separate study on motor learning, where they learned a digital mirror tracing task and a stepping task, but that study is beyond the scope of this thesis.

3.1.3. Sleep and cognitive assessments

The sleep diary, actigraphy, and cognitive tests (i.e., Psychomotor Vigilance Test (PVT), the Mnemonic Similarity Test (MST), and the Cambridge Neuropsychological Test Automated Battery (CANTAB) were the same as described above in Study 1.

3.2. Data analysis

The effects of total sleep deprivation on cognitive performance were assessed using independent t-tests run in Prism Graphpad 9, comparing the sleep deprivation and rested conditions. Shapiro-Wilk's tests assessed the normality of the data. Normal data are presented as mean ± SEM. For non-normal data, we ran the Mann-Whitney U test and reported data as median and interquartile range (IQR). The sleep measures used in the first study were used in this second experiment as well, using ActStudio Software (Condor Instruments, version 1.0.23) for analysis. In addition, all the cognitive tests and outcome measures used in the first study were included in this sleep deprivation experiment. Two-tailed statistical tests were used and Bonferroni correction was applied for analyses including sleep and cognitive measures to correct for multiple comparisons.

3.3. Results

3.3.1. Sample characteristics

Five rested participants were excluded from all analyses; 2 were excluded due to having a mental health condition and 2 were excluded due to missing actigraphy data, and 1 was excluded due to trans meridian travel within the past month (i.e., across multiple time zones), leaving 27 rested participants (age range: 18-25, mean age: 20.19

± 1.94, 14 females) included in one or more analyses. Three participants were excluded from all MST analyses due to response bias, and no participants were excluded from CANTAB. No participants were excluded from the PVT. In the sleep-deprivation condition, one participant withdrew from the study due to becoming ill, one student was excluded from all analyses due to not complying to the protocol, and one participant was excluded due to poor cognitive test performance (i.e., showing no concentration during the CANTAB, and demonstrating poor LDI performance on the MST) leaving 13 participants (age range: 18-34, mean age: 24.38 ± 4.96, 6 females) included in one or more analyses. Four sleep deprived participants were excluded from all MST analyses due to response bias or a REC score below the cut-off point (i.e., .50). No participants were excluded from the CANTAB, and no participants were excluded from the PVT. Included participants' demographic information is displayed in Table B.24.

3.3.2. Cognitive test results

Participants in both conditions were tested on the MST measuring pattern separation, and the CANTAB, measuring a range of cognitive functions and pattern separation processes included. The NASA-PVT assessing reaction time and sustained attention was used as a positive control measure.

NASA- PVT

Table B.25 in Appendix B displays independent t-tests comparing participants on the PVT total lapses, 10% fastest RT, 10% slowest RT, Mean 1/RT, and cognitive slowing. As shown by the table, there were no significant differences between the sleep deprived and rested participants on the PVT measures. Graphical representations for PVT slowest 10% RT (Fig. 3.1) and PVT total lapses (Fig. 3.1) show that rested participants exhibited non-significantly stronger performance. The data are affected by a few outliers. Performance differences seem to be related to higher performance variability in the sleep deprived group.

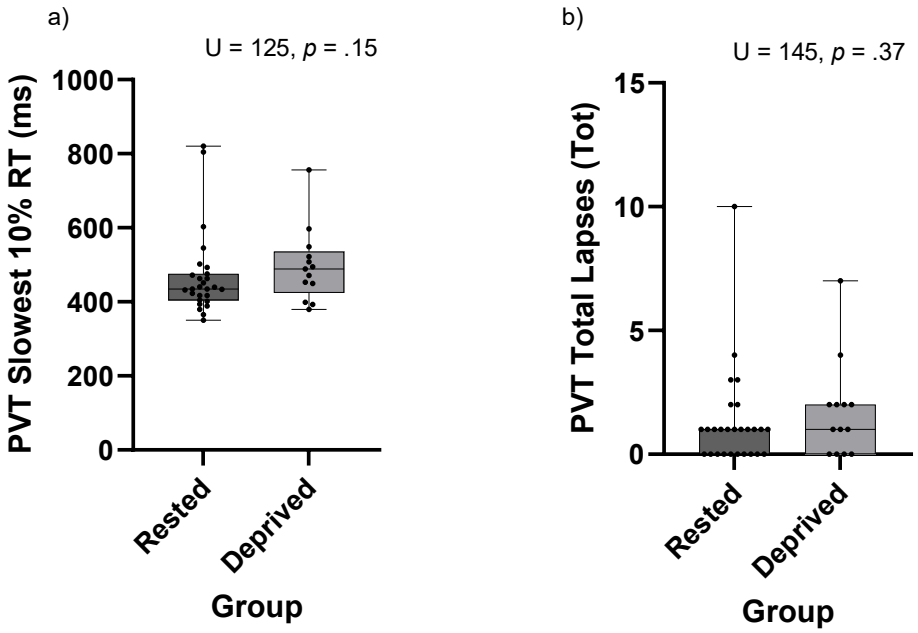

Figure 3.1. a) Boxplot comparing rested and sleep deprived participants' performance on PVT slowest 10% RT b) Boxplot comparing rested and sleep deprived participants' performance on PVT total lapses.

MST

Table B.26 displays independent t-tests comparing participants on LDI, REC, and the 5 lure bins. When applying the Bonferroni correction (≤.007), no comparisons reached statistical significance. However, comparison on the L2 was close to a significant result [t(30)= 2.28, *p* = .03], and graphical display shows that the sleep deprived group exhibited inferior performance compared to the rested group (Fig. 3.2). However, the results were not significant.

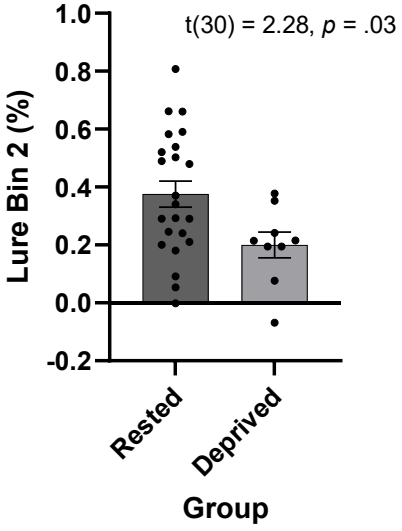

Figure 3.2. Bar graph comparing rested and sleep deprived participants' L2 performance.

CANTAB

The rested and sleep deprived participants were compared on the different CANTAB measures and the results are displayed in Table B.27 in Appendix B. As shown in Table B.27, there were no significant differences between participants' CANTAB performance when applying the Bonferroni correction ($p \leq .003$). Graphical display of the data showed that rested participants committed more errors on the SWMBE (SWM Between Errors) (Fig. 3.3) and on the SWMBE8 (SWM Between Errors, 8 boxes) (Fig. 3.3) compared to sleep deprived participants, but the difference was not significant. Rested participants also had slightly better strategy compared to deprived participants (Fig. 3.3). Table B.27 shows that sleep deprived participants scored better on the PALFAMS (PAL First Attempt Memory Score) and also showed a lower score on the PALTEA (PAL Total Errors Adjusted) compared to the rested participants, but this difference was not significant. Table B.27 also shows that the sleep deprived participants showed longer latency on most of the DMS sub-measures compared to the rested participants, however, the differences were not statistically significant.

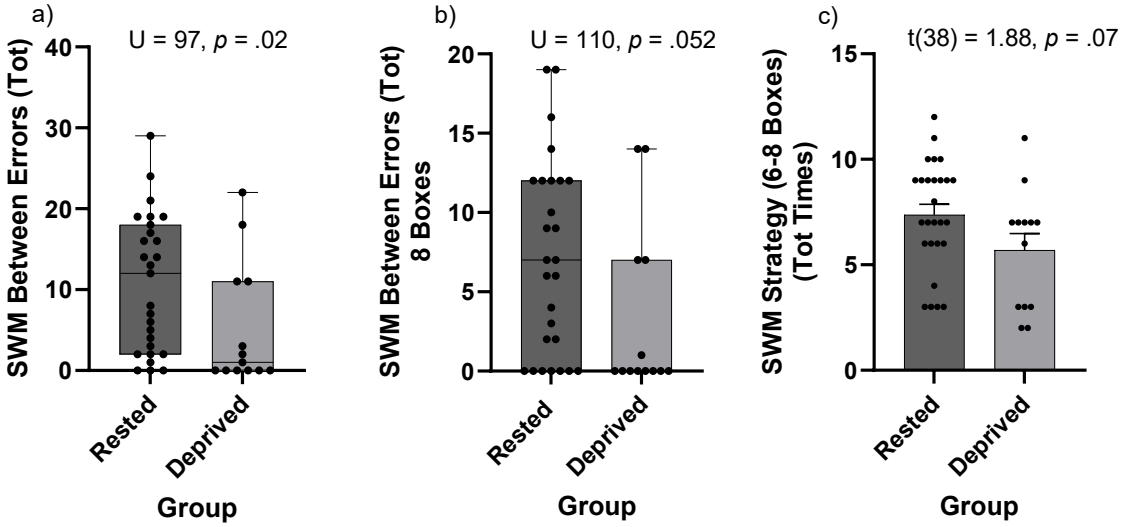

Figure 3.3. a) Boxplot comparing rested and sleep deprived participants' performance on SWMBE b) Boxplot comparing rested and sleep deprived participants' performance on SWMBE8 c) Bar graph comparing rested and sleep deprived participants' performance on SWMS.

3.4. Summary

In this sleep deprivation experiment, we examined how a night of total sleep deprivation would affect cognitive performance on the MST and CANTAB, and on the positive control, the PVT. On the MST, rested participants exhibited a higher pattern separation score compared to the sleep deprived participants. However, differences were not statistically significant. On the CANTAB, the rested participants also showed shorter latencies on most of the DMS sub-measures compared to the sleep deprived participants, but this was not statistically significant. Some of the results on other CANTAB tests contradicted our predictions that the rested participants would exhibit superior performance compared to the sleep deprived participants. For example, graphical display showed that the sleep deprived participants showed fewer errors (not statistically significant) on the SWM (i.e., SWM Between Errors and SWM Between Errors, 8 boxes) and PAL (PAL First Attempt Memory Score and PAL Total Errors Adjusted) compared to the rested participants. This might indicate that the sleep deprived participants may have recruited compensatory strategies to perform well despite being sleep deprived. Thus, overall, this study shows that MST and the CANTAB DMS may be more sensitive to total sleep deprivation compared to the other CANTAB sub-measures (i.e., PAL, SWM, and RTI).

Chapter 4.

General discussion

Across two experiments, we aimed to identify one or more sleep-dependent cognitive measures, using cognitive tests that were designed to detect the earliest cognitive changes associated with Alzheimer's disease. Our research studies examined the effects of sleep using a variety of cognitive tests including the MST and CANTAB. In addition, we were particularly interested in tests that tax pattern separation. Assessing how specific sleep parameters (total sleep time, sleep onset latency, sleep efficiency, and WASO) might be associated with pattern separation performance is a novel approach. Moreover, it can also provide more insight into how sleep quantity and/or quality affect episodic memory processes, which is among the memory systems that decline first in AD. As sleep often is disturbed in prodromal AD and MCI (Lloret et al., 2020; Zhang et al., 2019; Ju et al., 2014), identification of sleep dependent cognitive tests would help identify individuals who experience sleep disturbances and who might benefit from sleep promoting interventions. The prodromal AD phase represents an important time period for therapeutic interventions, such as sleep promoting interventions, considering that AD has not yet progressed to the stage of symptom onset (Soldan et al., 2016). Identifying cognitive tests most sensitive to sleep disruptions can also be used in the clinical trials as outcome measures when measuring the effectiveness of sleep-promoting interventions and how these interventions may aid cognitive functioning.

Dorrian et al. (2005) proposed criteria for what a measure should include in order to be appropriate as a sleep-dependent cognitive test. Ideally, a cognitive test that assesses the effects of sleep loss during waking performance should reflect aspects of cognitive function that is: 1) sensitive to the interaction between the endogenous circadian pacemaker and the homeostatic sleep drive, and 2) fundamental for different expressions of cognitive performance (Dorrian et al., 2005). The test also needs to be easily performed, be as brief as possible, be minimally influenced by learning processes, be valid and reliable, and should also provide outcome variables that are easy to interpret (Dorrian et al., 2005). We hypothesized that MST and the CANTAB DMS would meet these criteria. We wanted to implement cognitive tests that have been shown to be

sensitive to prodromal AD and MCI (e.g., CANTAB) and examine how sleep is uniquely related to performance on these tests.

4.1. Correlational study: Sleep

4.1.1. Actigraphy

We used objective activity data (i.e., actigraphy) to compare older and younger adults' rest-activity patterns to estimate total sleep time, sleep onset latency, sleep efficiency, and WASO. Sleep diaries were used to interpret the actigraphy data, such as bed and waketimes. We did not focus on the self-reported sleep data because it is not highly correlated with objective sleep measures, especially in older participants (Buysse et al., 2008).

Our results showed that the younger adults had significantly shorter sleep duration. Although the literature frequently suggests that sleep variables such as total sleep time declines in older age, it is important to note that younger adults may also experience disturbed or restricted sleep (Wei et al., 2021), likely due to external factors. In Wei et al.'s study, the younger adults had shorter sleep duration compared to both healthy older adult participants and older participants diagnosed with dementia. As our young sample included university students, it is likely that the shorter sleep duration overall in this sample can be explained by sacrificing sleep to study (Hershner & Chevin, 2014). In fact, research shows that 50% of college students report daytime sleepiness and approximately 70% do not attain sufficient sleep amounts (Hershner & Chevin, 2014; Van Dongen et al., 2003). Moreover, about 70.6% of college students report attaining less than the recommended 8-9 hours of sleep (Lund et al., 2010). In our study, actigraphy results indicated that the younger adults slept on average 6.44 hours, averaged across the 7 days of rest-activity recording. Occasionally, students may pull an "all-nighter", meaning that they stay awake for 24 hours or more. More frequently, students experience chronic partial sleep deprivation, which means that their sleep amounts are not sufficient to meet their sleep needs (Hershner & Chevin, 2014). This may also affect their academic performance (Curcio et al., 2006). Our finding that the younger adults exhibited shorter sleep duration on average can thus be explained by the homogeneity of the sample (i.e., being university students). Physiologically, young adults commonly also have a delayed circadian rhythm (Jenni & Carskadon, 2007). This may

lead to a preference for later bedtimes and need for a later wakeup time. However, as they may need to get up early in the morning to go to work or class, their total sleep time is likely to suffer as a consequence (Hershner & Chevin, 2014). Thus, younger adults often experience *social jetlag*, defined as the discrepancy between work and free days, between biological and social time (Wittman et al., 2009).

There were no differences between the younger and older adults in terms of WASO, sleep efficiency and sleep onset latency, which contradicts literature (Li et al, 2018; Mander et al., 2017; Ohayon et al., 2004). However, assessing sleep across 7 days may be too short in terms of detecting true differences in sleep quality and quantity between older and younger adults. On the other hand, research has shown that 7 days of actigraphy recording shows comparable results to longer periods of recording (e.g., 14 days), with subtle differences in total sleep time (Briscoe et al., 2014). Looking at the sleep onset latency in both groups, the latency was short. Another study using ActTrust watches obtained similar results for sleep onset latency (Albu et al., 2019). In general, research shows that actigraphy watches often underestimate sleep onset latency (Sivertsen et al., 2006; de Souza et al., 2003), as the watches may not be sensitive enough to detect wake when subjects are awake but motionless (Sadeh & Acebo, 2002). In terms of sleep and sex differences, there were no differences between females and males in the older adult sample. However, in the younger adult sample, we observed a significant difference between females and males in total sleep time where the females showed longer sleep duration. This is consistent with literature in that females exhibit longer objective sleep duration compared to males (Kováčová & Stebelová, 2021). On subjective measures, such as the Pittsburgh Sleep Quality Index (PSQI), females have also reported longer sleep duration (Fatima et al., 2016; Lindberg et al., 1997).

4.2. Cognitive performance

4.2.1. PVT

As the PVT has demonstrated in numerous studies to be sensitive to circadian rhythm misalignment and sleep loss, we administered the PVT to use the test as a positive control in both of our experiments. Specifically, we focused on the PVT measures total number of lapses, 10% fastest RT, 10% slowest RT, mean reciprocal

response speed, and cognitive slowing, as these have been shown to be most sensitive to sleep and sleep loss (Basner & Dinges, 2011; Arsintescu et al., 2019).

The results support the literature that 10% slowest RT and cognitive slowing are sensitive to different amounts of sleep (Basner & Dinges, 2011; Arsintescu et al., 2019). Proneness to lapses is also commonly reported in sleep deprivation studies (Basner & Dinges, 2011), however, we did not observe any clear relationship between any of the sleep parameters and lapse frequency in the correlational study. It is likely that the 5-min PVT is not long enough to lead to any attentional lapses compared to the 10-min PVT (Roach et al., 2005; Loh et al., 2004), and that more frequent lapses are associated with longer tasks (Lamond et al., 2008; Loh et al., 2004). This is referred to as the time-on-task effect (Lim & Dinges, 2008). However, as fatigue and sleepiness accumulate, more frequent lapses do occur during the 5-min PVT, like we observed in the sleep deprivation experiment (Lamond et al., 2008; Loh et al., 2004). The lack of relationship between lapses and sleep parameters in the older and younger sample may be explained by 1) the task was not long enough to lead to lapses, and 2) the subjects may not have been tired enough or accumulated enough sleep dept across the week in order to commit any lapses during testing. Overall, the results showed that there was a relationship between sleep and a few of the other PVT measures (i.e., cognitive slowing and slowest 10% RT). In the sleep deprivation study, there were no significant differences in PVT performance, but graphical display showed differences between the rested and sleep deprived group in terms of lapses and 10% slowest RT. The differences were due to more performance variability in the sleep deprived group and a few long lapses in the rested group, and were not statistically significant.

4.2.2. MST and pattern separation

We also aimed to examine how sleep and sleep loss affects performance on tasks measuring pattern separation performance. As previously discussed, sleep before encoding is important for efficient declarative memory performance (Yoo et al., 2007) and pattern separation (Poh & Cousins, 2018). Thus, pattern separation performance on the MST is likely to be superior in older and younger participants who are more rested, both quantitatively (i.e., total sleep time) and qualitatively (i.e., sleep efficiency and WASO) compared to older and younger participants who are less rested. In the sleep

deprivation study, MST performance is likely to be impaired in the sleep deprived compared to the rested group.

In the correlational study, graphical representation of the data showed that pattern separation performance exhibited sensitivity to total sleep time in the older adults, although the results were not statistically significant. Specifically, lure bin 1, which is the MST condition that taxes pattern separation the most, showed most sensitivity to total sleep time in that longer sleep duration was associated with superior performance compared to shorter sleep duration. In the younger adults, pattern separation performance also showed sensitivity to one of the sleep parameters. Specifically, lure bin 5 performance seemed to be most sensitive to WASO. In the sleep deprivation study, there were no significant differences between the groups. Graphical display shows that the rested group showed superior performance on the MST, especially on lure bin 2 compared to the sleep deprived group. However, this difference was not significant.

Previous studies have found that participants who are allowed to sleep show superior pattern separation performance compared to participants who are sleep-deprived (Saletin et al., 2016) or tested after a period of wakefulness (Hanert et al., 2017; Doxey et al., 2018; Cellini et al., 2020; Cellini, 2023). In the correlational study, our results go beyond these findings by further demonstrating that pattern separation performance is uniquely sensitive to sleep quantity and quality. There are a few different explanations for these findings.

First, one explanation is the effect of adenosine on cognitive performance, specifically, on hippocampal dependent memory (Porkka-Heiskanen et al., 1999). Adenosine accumulates within DG/CA3 and is derived from astrocytes and neurons (Saletin et al., 2016). Higher adenosine levels, which accumulate proportionally to the amount of time awake, may impair or inhibit hippocampal memory processes that are necessary for plasticity. Therefore, deficits in pattern separation performance may be explained by adenosine accumulation in the hippocampus and the basal forebrain.

Second, showing superior pattern separation performance after sleep supports sleep's role in the establishment of distinct representations for discriminative stimuli (Poh & Cousins, 2018; Kent & Mistlberger, 2017; Tononi & Cirelli, 2014; Gais et al., 2000; Yoo

et al., 2007). Specifically, as pattern separation takes place during encoding, sleep before encoding may lead to superior pattern separation performance compared to participants who have slept less. Our findings go beyond these data showing that there is a unique relationship between total sleep time and ability to distinguish between highly similar lures and target images, especially in the older adults. Sleep, and particularly N3, may help the desaturation or downscaling process of synapses that were active during input encoding in the waking state, thus increasing or regaining capacity to encode new information (Tononi & Cirelli, 2006, 2014). However, as we also did not measure the different sleep stages directly, such as the amount of N3, this explanation for our findings remains speculative.

We found a stronger relationship between sleep and pattern separation performance in the older compared to the younger adults, which could be explained by older adults needing more sleep to combat age related effects on stimuli discrimination performance (Van Dongen et al., 2003). Our sample of younger adults was homogenous in that it included only university students. University students frequently sacrifice sleep to study thus may be more able to perform well despite sleep loss (Hershner & Chevin, 2014). Based on graphical inspection, the younger adult data also showed more spread compared to the older adult data, likely indicating more interindividual differences in the resilience and vulnerability to sleep loss (Mu et al., 2005).

Research has identified interindividual and age differences in the sensitivity to sleep loss on hippocampal-dependent learning (Lee et al., 2020; Saletin et al., 2016). Using mouse models in a sleep deprivation experiment, Lee et al. showed that fast learning mice that were sleep deprived expressed higher levels of BDNF, among others, compared to sleep deprived mice that were slow learners. As BDNF is involved in neuroplasticity and has been shown to be important for DG-dependent pattern separation in rodents (Bekinschtein et al., 2013), a higher level of BDNF in sleep deprived mice helped hippocampal-dependent learning despite the impairing effects of sleep loss. In human aging, levels of BDNF decline (Erickson et al., 2010). That might also explain why older adults show more sensitivity to sleep loss during a hippocampal dependent task like the MST. Furthermore, using MST, Saletin et al. showed that structural morphology of human hippocampal subfields contributed in determining sensitivity to sleep loss. Specifically, individuals with a larger DG/CA3 subfield seemed to be more vulnerable to the deteriorating effects of sleep loss.

Research previously conducted on sleep and pattern separation performance included a retention interval between encoding and the memory test session (Doxey et al., 2018; Hanert et al., 2017; Cellini, 2023). In these studies, one group was tested in the morning after a night of sleep (i.e., encoding took place at night) and a second group was tested in the evening after a day of wakefulness (i.e., encoding took place in the morning). Across the studies, it was shown that sleep stabilized pattern separation performance, leading to a stronger performance in the sleep group compared to the wake group. We did not include a retention interval between the encoding phase and test phase, thus, participants were tested immediately following encoding. It is likely that our participants may have showed a stronger pattern separation performance if they were allowed to sleep post encoding. As sleep also is important for consolidation, we can hypothesize that our participants would have benefitted from sleep after encoding (Rasch & Born, 2013).

Furthermore, in the correlational study, recognition memory performance did not show a relationship with any of the sleep parameters. In the sleep deprivation study, there were no differences between the groups on REC performance. Other studies have also found that recognition memory is robust to the effects of sleep and sleep loss in younger adults (Cellini, 2023; Mander et al., 2011; Davidson et al., 2021). However, Hanert et al. (2017) found that recognition memory scores were significantly higher after a night of sleep compared to after a day of wakefulness. Other studies have also identified effects of sleep deprivation on recognition memory, where memory was significantly impaired in the sleep deprived group (Yoo et al., 2007; Cousins et al., 2019). However, Saletin et al. (2016) found that sleep had a larger impact on pattern separation performance compared to recognition memory. These inconsistent results between previous literature may again be explained by interindividual differences in vulnerability and resilience to sleep loss. In our study, the finding that sleep and sleep deprivation did not seem to impair performance in our studies can also be due to the suggestion that recognition memory has not been considered to be hippocampus dependent like pattern separation (Stark et al., 2013; Abel et al., 2013). Research suggests that recognition memory might depend more on the perirhinal cortex (Ameen-Ali et al., 2021) and the CA3 (Dillon et al., 2017), as both areas have been found to process recognition and familiarity. CA3 has also been linked to recognition memory on the MST (Dillon et al., 2017). It is likely that recognition and familiarity memory is less sensitive to sleep loss as

image detail encoding is not crucial for later successful recollection but rather overall familiarity and gist (Koutstaal et al., 1999, 2001). Similar explanation can also explain why we did not see age related declines in recognition memory in the older adults (Stark et al., 2019; Stark et al., 2013; Stark & Stark, 2017) as CA3 has been shown to exhibit less age-related declines compared to other hippocampal regions (e.g., DG) (Dillon et al., 2017).

In the clocklab analysis, there were significant relationships between MST measures and the circadian parameters in both the older and younger sample. In the younger adult data, amplitude showed a positive correlation with LDI, lure bin 2, and lure bin 4. A higher amplitude suggests a strong and robust circadian rhythm, whereas a low amplitude indicates a less distinct and weaker circadian rhythm (Rabinowitz et al., 2022). According to our data, superior performance on pattern separation was related to a higher amplitude compared to a lower amplitude. This can indicate that individuals with higher amplitude perhaps had more consolidated sleep, leading to more alertness during the day, which may have led to improved cognitive performance (Rabinowitz et al., 2022). In the older adult data, we did not see any significant relationships between amplitude and any of the MST metrics. Aging is associated with amplitude reductions, which means that there are decreases in the magnitude of difference in activity between rest and active phases (Rabinowitz et al., 2022). Therefore, one could expect to see significant relationships between amplitude and memory performance in the older adults; however, the relationships were not significant.

In the correlational study, we also showed that the younger adults exhibited superior pattern separation performance compared to the older adults. This is consistent with previous findings (Stark et al., 2015; Stark, Yassa, & Stark, 2010; Toner et al., 2009). Age-related changes in hippocampal activity may lead to inability to pattern separate comparably to younger adult performance. For example, research shows that declines in different hippocampal and non-hippocampal volumes in older adults may predict lure discrimination deficits on the MST (Stark & Stark, 2017). Furthermore, aging associated rigidity that occurs in the hippocampal regions, such as the DG and the perforant path, may also explain why older adults tend to show lower pattern separation performance compared to younger adults (Yassa et al., 2011a, 2011b). The integrity of the perforant path was strongly correlated with the extent of dendritic rigidity in the left

DG/CA3, and these findings correlated with the older adults' pattern separation performance on the MST (Yassa et al., 2011a, 2011b; Bennett et al., 2015).

It should also be mentioned that the degree of input similarity is processed differently in older adults compared to in younger adults (Yassa et al., 2011a, 2011b; Lacy et al., 2011). Lacy et al., 2011 investigated how younger and older adults' DG/CA3 regions responded to lure images split into different similarity bins. In the younger adults, even minor changes in input (i.e., increases in similarity) led to higher activity in the left DG/CA3 region, and remained in high activity state as similarity increased. In contrast, the older adults' left DG/CA3 region exhibited diminished pattern separation activity on the highly similar lures and only showed elevated activity on the highly dissimilar lures. This indicates the representational rigidity or resistance to change and remapping that occurs in older age and might explain why older adults may find it difficult to perform pattern separation (Yassa et al., 2011a). The older adults in our study showed lower pattern separation performance across the five lure bins compared to the younger adults, which could be explained by lower pattern separation activity in DG/CA3 to that of the younger adults. However, most of the performance differences were non-significant.

It is worth noting that in our younger adult sample in the correlational study, female participants were significantly disproportionately represented compared to male participants. It was not in our intention to recruit a higher proportion of females and this was entirely a byproduct of the number of participants who expressed interest in the study and the participant population we had available. Previous studies including the MST and equal gender distribution did not notice gender differences in test performance (Stark et al., 2015). In our study, we did not notice any differences between the sexes in the older or younger adult sample on the MST. However, research on episodic memory has found that females' episodic memory and autobiographical recall performance is superior compared to males' performance (Andreano & Cahill, 2009).

It should also be mentioned that we did not compute pattern completion scores as researchers have questioned the MST as a valid and accurate pattern completion measure (Liu et al., 2016). Both pattern separation and pattern completion are computational processes relying on the hippocampal network. However, whereas pattern separation relies on the DG, pattern completion is associated with the recurrent

collateral network CA3 and refers to transforming degraded representations into previously stored representations by filling in missing information (Yassa & Stark, 2011a; Stark et al., 2013). It may therefore be involved in both pattern separation and pattern completion, depending on the task. As pattern separation is computed at the time of encoding and storage making noisy inputs distinct, pattern completion is performed during retrieval so that a complete pattern can be recalled based on an incomplete input (Rolls, 2010; Hunsaker & Kesner, 2013).

Researchers using the MST have calculated pattern completion performance as judging similar lures as "old" (Yassa et al., 2011a; Toner et al., 2009). Some have argued that pattern separation and pattern completion trade-off in that scoring higher on pattern separation would automatically indicate a lower pattern completion score, and vice versa (Molitor et al., 2014). Especially older adults would show compensatory increases in pattern completion when pattern separation performance fails. However, research has found that older adults who show impaired pattern separation do not always exhibit superior performance on pattern completion. For example, patients with AD or hippocampal damage do not show increased pattern completion, which indicates that the two processes are not dependent on one another (Ally et al., 2013). Moreover, judging similar lures as "old" does not indicate pattern completion (Hanert et al. 2017; Hunsaker & Kesner, 2013; Liu et al., 2016). This is because we cannot be fully certain how much pattern completion contributes to discrimination performance if *similar* rather than *incomplete* stimuli are presented to participants (Liu et al., 2016). Thus, any false alarm rate could be explained by a weak initial encoding process instead of pattern completion performance (Molitor et al., 2014). Therefore, we should not think of the inverse of LDI as pattern completion.

4.2.3. CANTAB, DMS, sleep, and pattern separation

Our correlational study also aimed to identify associations between sleep quantity (i.e., total sleep time) and sleep quality (i.e., sleep efficiency and WASO) and the different CANTAB sub-measures. The sleep deprivation study aimed to investigate how total sleep deprivation affected cognitive performance, including CANTAB. We were particularly interested in the CANTAB DMS measure as it includes components that resemble pattern separation performance, in addition to PAL, which also relies on MTL function. Both DMS and PAL have shown strong sensitivity to prodromal AD and MCI,

and also hippocampal damage (Fowler et al., 1997; Owen et al., 1995; O'Connell et al., 2004; Robbins et al., 1994; Blackwell et al., 2003; Fowler et al., 1997; Gould et al., 2005; Lee et al., 2003; Lenehan et al., 2016; de Jager et al., 2005; Saunders & Summers, 2010).

DMS

In the correlational study, there were no associations between the DMS measures and the sleep parameters. In the younger adult sample, DMSML12 (DMS Mean Correct Latency, 12 seconds delay) showed a non-significant relationship with sleep efficiency. In the older adult sample, correlations between DMSML4 (DMS Mean Correct Latency, 4 seconds delay) and sleep efficiency and WASO were significant. Of the good and bad sleepers, the DMS results did not reveal any significant differences between the groups in either sample. However, looking at table display, the younger adults who were good sleepers in terms of both sleep efficiency and total sleep time, seemed to show longer latency on the DMS compared to the bad sleepers (Table B.20 and B.21). In contrast, the older adult good sleepers (sleep efficiency) showed shorter latency on the DMS measures compared to the bad sleepers (Table B.23). This might indicate that older adults are in a stronger need of sufficient sleep in order to perform well on pattern separation, whereas younger adults characterized as bad sleepers might have recruited compensatory strategies in order to rescue task performance.

Overall, the results suggest that higher sleep efficiency and shorter WASO were associated with shorter latency in the younger and older participants' responses, thus, more rested participants needed less time to remember the correct pattern, especially among the older adults. This indicates that being more rested aids pattern separation performance. In a different study, Waller et al. (2016) found a significant negative correlation between DMS performance and subjective sleep onset latency in both cognitively improved and impaired males. There were no correlations with subjective sleep duration. However, the authors did not specify which two DMS measures were included in the analyses. In Gnoni et al.'s (2023) study on obstructive sleep apnea and CANTAB, the authors used the DMS measure *DMS median latency (all delays)*, which is similar to our DMS measure, the DMSMLAD, except that it focuses on the median instead of the mean. OSA patients in Gnoni et al.'s study showed lower median

response time and also less spread in the data compared to controls, according to graphical display.

In the sleep deprivation study, there were no significant differences between the rested and deprived participants on DMS performance. However, looking at table display of the data (Table B.27 in Appendix B), it is clear that the deprived participants in general needed more time to process and remember the correct patterns. One other study investigated the effect of total sleep deprivation on CANTAB performance in healthy young males focusing on all 41 DMS sub-measures (Csipo et al. 2021). There were no performance differences between rested and sleep deprived participants on any of the DMS measures. Overall, our results suggest that the DMS may be sensitive to sleep, especially sleep quality in the correlational study (i.e., WASO and sleep efficiency) compared to sleep quantity (i.e., total sleep time). However, looking at Table B.27, total sleep deprivation seemed to affect performance on the DMS by slowing the responses. As only a few studies on sleep and sleep loss have included the DMS, it is difficult to draw strong conclusions about this measure. Future studies on sleep and cognitive performance could implement all of the 41 DMS measures and examine how different levels of sleep quantity, such as sleep restriction, and quality, such as sleep fragmentation, affect DMS performance.

PAL

It is suggested that PAL performance is sensitive to the AD pathological markers, such as neurofibrillary tangles (Blackwell et al., 2004). PAL has predicted individuals' deterioration in global cognitive functioning over the next 8 months, thus is able to detect cognitive decline before symptoms become apparent (Blackwell et al., 2004). PAL also predicted subsequent cognitive deterioration in individuals who believed their health and cognition were intact and comparable to peers (de Jager et al., 2005).

In the younger adult sample, none of the correlations between the PAL sub-measures and the sleep parameters were statistically significant. The data is characterized by high clustering and heteroscedasticity (i.e., affected by outliers) which may have influenced the relationships observed. In the older adult sample, no correlations reached statistical significance, however, the correlation between PALTEA2 (PAL Total Errors Adjusted, 2 shapes) and WASO and the negative correlation between sleep onset latency and PALTEA6 (PAL Total Errors Adjusted, 6 shapes) was close to a

significant value. The results indicated that longer sleep onset latency was associated with improved PALTEA6 performance. The PALTEA6 has been of interest in other studies (Blackwell et al., 2004; Swainson et al., 2001; Lee et al., 2003; O'Connell et al., 2004; de Jager et al., 2002) as it may be the PAL measure that is most predictive of future AD diagnosis (Blackwell et al., 2004). Short sleep onset latency has been found to be related to increased sleep dept, which is the overall effect of not getting enough sleep (Carskadon, 1986). As participants with longer sleep onset latencies showed less errors on the PALTEA6 compared to participants with shorter latencies, this might indicate that being rested is associated with fewer memory errors. No other sleep measures showed a relationship with PALTEA6. Of the good and bad sleepers in terms of sleep efficiency and total sleep time in both participant samples, there were no significant differences in PAL performance. In the sleep deprivation study, however, graphical display of the data showed performance differences between the groups, although not statistically significant. Specifically, sleep deprived students showed a better performance on the PALFAMS (PAL First Attempt Memory Score) and a lower error score on the PALTEA (PAL Total Errors Adjusted) compared to the rested participants. This is consistent with Csipo et al.'s (2023) study in that they found no effect of total sleep deprivation on PAL measures. Additionally, Gnoni et al. (2023) also did not observe any differences between controls and OSA patients (mild and severe) on the PAL measures PALFAMS and PALTEA. However, their sample sizes were small (Controls: 7; mild OSA; 16; severe OSA; 11), which may have led to reduced statistical power to detect performance differences. Waller et al. (2016) found a significant negative correlation between PAL and sleep onset latency. The authors did not specify which PAL measures they focused on. Last, Thomas et al. (2019) found no differences on PAL performance (PALTEA) between maritime pilots who frequently experience sleep disturbances, and controls.

The PAL is thought to rely on parahippocampal regions, such as the perirhinal and entorhinal cortex, and subregions of the hippocampus proper (Kesner, 2013; Hunsaker et al., 2006). As sleep before encoding is important for encoding and also later retrieval to be successful, sleep deprivation may lead to deficits in PAL performance by impairing cellular processes in these areas, such as synaptic downscaling as previously discussed (Tononi & Cirelli, 2014; Vyazovskiy et al., 2008). However, in our studies, we did not observe any effects of sleep loss on PAL performance.

5-Choice RTI

The 5-Choice RTI measures divided attention, which is one of the first attentional functions to decline in prodromal AD (Perry & Hodges, 1999). In the RTI task, we did not observe any significant correlations between sleep and RTIFMMT (RTI Mean Five-Choice Movement Time) in the older or younger sample, nor between good and bad sleepers in terms of total sleep time and sleep efficiency in either sample. The RTIFMMT measures the time it takes to release the button at the bottom of the screen and select the target button at the top of the screen. The sleep deprivation experiment also did not reveal any significant differences between the rested and sleep deprived group. Looking at Table B.27, the groups in the sleep deprivation study showed similar performances. Csipo et al. (2023) found that a night of total sleep deprivation significantly increased RT in the sleep deprived group. In Waller et al. (2016)'s study, RTI showed a significant negative correlation with sleep onset latency in the combined sample overall. However, the authors did not specify which RTI measures were used. In Gnoni et al.'s (2023) study, there was a significant difference between reaction times in controls and in patients with severe OSA, and between patients with mild OSA and severe OSA. There were no significant correlations between controls and patients with mild OSA. In Thomas et al.'s (2019) study, the authors used the RTI measure *FMDT*, which is the median duration it took for a subject to release the response button after the presentation of a target stimulus. There were no performance differences between maritime pilots, who frequently experience sleep disturbances, and controls. Across the different studies' and our experiments' results, the findings seem to be inconsistent. According to the study findings, it appears that more severe sleep disturbances, such as in severe OSA and after total sleep deprivation, may induce more impairments in performance compared to less severe sleep disturbances, such as in mild OSA. However, in our 24 h sleep deprivation study, we did not detect any strong performance differences, perhaps due to the resiliency in students when facing sleep loss, which was seen in maritime pilots who also frequently are sleep deprived (Thomas et al., 2019).

SWM

The SWM taxes working memory processes, and depends on attention and executive functions to operate on incoming information (Sabahi et al., 2022). In prodromal AD and MCI, working memory has been found to be impaired, which makes it

a useful measure for identifying MCI and prodromal AD (Kirowa et al., 2015; Gagnon et al., 2011).

Working memory has also been shown to be sensitive to short-term sleep deprivation (Peng et al., 2020; Mu et al., 2005). In our correlational study, we observed significant correlations between SWMBE6 and sleep efficiency and WASO in the younger adult data. There were no significant correlations between the SWM sub-measures and the sleep parameters in the older adult data. In terms of good and bad sleepers there were no differences on working memory performance in the older or younger adults. When looking at the graphical display for the younger adult data, some of the bad sleepers, in terms of sleep efficiency, showed non-significantly more errors on the SWMBE (SWM Between Errors), SWMBE6 (SWM Between Errors, 6 boxes), and SWMBE8 (SWM Between Errors, 8 boxes) compared to good sleepers. In the sleep deprivation experiment, some rested participants showed more errors on the SWMBE, and SWMBE8, but better performance on the strategy measure, the SWMS (SWM Strategy, 6-8 boxes), compared to the deprived participants, but this was not statistically significant. The finding that some of the participants in the sleep deprivation experiment showed better performance on some of the working memory measures (i.e., SWMBE and SWMBE8) compared to the rested participants, might indicate that they likely recruited compensatory strategies to perform well on this task. The fact that some of the bad sleepers in the correlational study showed worse performance on the same measures than the sleep deprived participants (no statistically significant differences) in the sleep deprivation study is interesting. It might suggest that the more sleep debt accumulation, the more compensatory strategies (e.g., additional brain regions) are recruited, which may be beneficial for task performance. Previous studies have shown that complex tasks, such as working memory tasks, might not be as sensitive to sleep loss as less complex tasks, as participants are likely to exert more effort during complex task performance (Ma et al., 2015; Drummond et al., 2004, 2005; Mu et al., 2005). This is consistent with some other CANTAB studies showing that complex task performance was not affected by sleep loss (Thomas et al., 2019; Csipo et al., 2023; Gnoni et al., 2023). This is also inconsistent with 2 other studies showing that SWM performance (i.e., SWMS and SWMBE) in OSA patients (Naëgelé et al., 2006) and in insomnia patients (SWMBE) (Edinger et al., 2021) was more impaired than in healthy controls.

Overall, results in other studies are inconsistent on SWM performance, and we see similar inconsistent results in both of our studies, perhaps due to compensatory strategies. On simpler, more monotonous tasks (e.g., PVT), effects of sleep deprivation tend to be stronger, as these tasks rely on sustained attention and speed of performance, which is sensitive to sleep loss (Dorrian et al., 2005). In addition, complex tasks that do not rely on speed (e.g., SWM) makes it easier to allocate cognitive resources to perform accuracy, referred to as speed-accuracy trade off (Robbins et al., 1994). A different explanation is that some individuals may be more sensitive to the effects of sleep deprivation on working memory than others (Mu et al., 2005).

4.2.4. Clocklab and CANTAB

Our data revealed a significant correlation between DMSML0 (DMS Mean Correct Latency, 0 s delay) and acrophase in the younger adult data. The acrophase indicates the time of maximum activity counts over 24 h (Rabinowitz et al., 2022) and a positive correlation may suggest that a later acrophase is associated with longer response latency on this DMS sub-measure. We also observed a significant correlation between acrophase and SWM (SWMBE4; SWM Between Errors, 4 boxes) in the older adult sample. The positive correlation between acrophase and between errors on the SWM (SWMBE4) might indicate that those with a later peak made more errors on the SWM, whereas those with an earlier peak, made less errors. This can be explained by older adults being most alert in the morning compared to later in the day (Knight & Mather, 2013), and that a later acrophase might be associated with declines in cognitive performance.

In all CANTAB tasks, younger adults significantly outperformed the older adults. In general, younger adults showed faster response times on the DMS (Robbins et al., 1994) and RTI, and fewer errors on the SWM and PAL. In both younger and older participants, latency became longer as a function of delay on the DMS. In terms of sex differences, our results did not reveal any significant differences between the sexes in either group. However, based on table display (Table B.15 and B.16), we can see that both younger and older females showed somewhat faster response latency on the DMS sub-measures compared to males. This is consistent with another study, which found the same result on the DMSMLS (DMS Mean Correct Latency, Simultaneous) (Robbins et al., 1994).

4.2.5. MoCA

The MoCA, developed by Nasreddine et al. (2005), is a valid measure designed to detect MCI. The MoCA assesses attention, executive functions, language, calculation, orientation, conceptual thinking, and visuoconstructional skills. Our results in the correlational study showed significant relationships between the MoCA total score and several of the PAL and SWM measures. This is consistent with previous studies, especially for the PAL (Hicks et al., 2020). Hicks et al. showed that PALTEA showed a strong negative correlation with the total MoCA score and also had 92% sensitivity and 86% specificity to detect AD. Moreover, PAL has also been shown to be a stronger predictor of future cognitive decline compared to the Mini Mental Status Exam (MMSE), which is a commonly used method to detect AD related impairments (O'Connell et al., 2004). The SWM, which is associated with frontal lobe function and working memory, also showed significant correlations with the MoCA total core. Thus, our research has provided further support for the use of CANTAB as a measure of deficits in cognitive performance, perhaps related to cognitive decline. However, it should be noted that none of our older participants were drawn from a clinical population, nor were the tests used (i.e., MoCA and CANTAB) used for screening or diagnostic purposes. Thus, our findings should be treated with caution as we also will not be doing participant follow-up to assess future cognitive performance and decline.

4.3. Limitations

When interpreting the results of the research, there are several limitations to consider. First, the generalizability of our younger adult samples in both studies may be limited in that the groups of participants were university students, thus exhibited a high degree of homogeneity. University students frequently have irregular work, study, and sleep schedules, which may not be generalizable to younger adults in the population who are not attending university. This may also have masked true differences between the younger and older participants' sleep and circadian patterns. Furthermore, the generalizability of the middle-aged and older adults should also be interpreted with caution. More than half of our sample was recruited via REACHBC, which is an online provincial platform that connects residents of British Columbia with health research opportunities. As the platform includes potential participants who already are interested

in research participation and know what research entails, the sample may not be generalizable to other potential participants who might be less experienced as a participant. Second, it should be noted that one older participant dropped out of the study during the first meeting as they did not want to wear the watch on their non-dominant wrist, which indicates that the watch wearing may have been inconvenient for some. For example, one other middle-aged participant was excluded after their data had been collected due to not wearing the watch at night. In the younger adult sample, one participant did not wear the watch for almost the total duration of the watch wearing period, and several participants indicated in their sleep diaries that the watch was uncomfortable to wear. It can be questioned whether willingness to comply with watch wearing represents a different population compared to participants who choose not to. The same can be speculated about the cognitive test results in that poor results, for example on the MST, may also have been due to not putting in effort in task performance. Third, as we ran multiple tests in the 2 studies, our sample sizes may have been too small to detect differences between the groups. For example, in our sleep deprivation study, the sleep deprivation group included only 13 participants which may have reduced statistical power. Fourth, in the correlational study, we are unaware whether the different performances may have been influenced by caffeine intake as we did not control for caffeine consumption. As caffeine is an adenosine-inhibitor, any effects of poor night time sleep may have been masked by the effects of caffeine (Reichert et al., 2022). Research has found that caffeine does influence cognitive performance (Hershner & Chervin, 2014) such as pattern separation measured using the MST (Borota et al., 2014). However, this study did not include any form of sleep deprivation. Fifth, on the PVT, we did not observe any strong relationships between the sleep parameters and lapse performance. It is likely that the 5-min PVT was too short (Lamond et al., 2002; Roach et al., 2005; Loh et al., 2004), especially in the younger adults, to detect effects of sleepiness despite being validated against the 10-min PVT (Lamond et al., 2008; Loh et al., 2004; Roach et al., 2006; Honn et al., 2015; Thorne et al., 2005; Lamond et al., 2005; Thompson et al., 2022; Lamond et al., 2002; Roach et al., 2005; Arsintescu et al., 2017; Arsintescu et al., 2019; Thompson et al., 2016; Thompson et al., 2019). Further, using actigraphy has different limitations. Although it has been validated against polysomnography, it is important to remember that activity thresholds can only estimate sleep and that actigraphy may overestimate total sleep time and underestimate sleep onset latency. Therefore, our sleep and wake estimations

may not be precise (Pollak et al., 2001). Last, using acrophase in non-continuous activity data also poses limitations. Acrophase estimations are based on the assumption that circadian rhythms follow a sinusoidal pattern (Lee et al., 2004). However, not all biological rhythms exhibit a sine wave. For example, bed and wake times in addition to activity levels do not follow a sine wave pattern. Thus, deviations from this assumption may affect the accuracy of our acrophase estimates. Therefore, our acrophase results should be interpreted with caution.

In terms of other explanations for the different MST results that we see, there are several other ways to explain our findings. For example, inefficient encoding of images during MST's encoding phase could be due to deficits in memory-related eye movements. This could perhaps lead to impaired memory of object details (Molitor et al., 2014; Kafkas & Montaldi, 2011; Hannula & Ranganath, 2009; Ryan et al., 2022). For example, in an eye-tracking study, Molitor et al. (2014) found that younger adults who fixated less on images in MST's encoding phase showed a higher number of false alarms compared to participants who made more fixations. Based on this research, it is possible that the older adults in our study may have performed less efficient fixations during image encoding compared to the younger adults, thus were less able to properly encode image details. In addition, we did not perform any form of vision checks in either sample, which may have influenced our results.

It should also be noted that button press responses during the MST might be difficult for older adults to coordinate (Stark et al., 2015). Stark et al. (2015) argue that lure discrimination deficits in older adults may be due to issues in their use of the "similar" response and not in issues in processing the lure images. It is likely that older participants may be less willing to use the response as it may be unfamiliar, or that they set a different threshold for when the similar response can be used. However, when changing task instructions to promote gist (i.e., old) and veridical (i.e., new) responses, the older adults still seem to struggle with the "similar" response (Stark et al., 2015). The same finding has been observed when changing the MST to self-paced, where the older adults have more time to choose a response, instead of the computerized version. However, it is also likely that age-related declines in hippocampal subregions associated with pattern separation may explain why they find the "similar" response difficult to use.

Chapter 5.

Conclusion and future directions

In the experiments presented in this thesis, we examined different cognitive tests to identify a sleep dependent cognitive measure. In terms of the effects of sleep on cognitive performance, the present study found that sleep efficiency and WASO were more related to cognitive performance compared to total sleep time. This has been found in other studies on the effects of sleep on cognitive performance (Blackwell et al., 2006; Gnoni et al., 2023). Thus, these findings may indicate that the most important sleep measures might be the amount of unwanted sleep disruptions or intruding wakefulness experienced, compared to the total amount of sleep that the individual obtains. This is also related to insomnia research and treatments, which commonly seek to decrease time spent in bed, thus increasing sleep efficiency. However, we did observe a strong relationship between total sleep time and pattern separation in the older adults. Therefore, future studies should look more into the different actigraphy sleep parameters and examine which are most associated with different forms of cognitive performance, such as pattern separation.

Looking back at Dorrian et al.'s (2005) suggestions for what an appropriate sleep measure should include, it is clear that CANTAB may be a useful tool to study sleep. Specifically, CANTAB may be suitable as a battery to measure sleep as it is easily performed, has tasks of variable durations, is minimally influenced by learning processes, and in addition, generates data that are easy to interpret and utilize. As it is important that tasks measuring the effects of sleep loss on cognition include sustained attention demands and are not too complex, CANTAB tasks that meet these demands would be beneficial. The MST, in comparison, includes a sustained attention component, nor is it too complex as it can be adjusted in terms of speed and number of presented stimuli. MST has also been validated for use in clinical research (Stark et al., 2019). However, adjustments to task format could be examined, such as implementing an MST touch screen version for iPads with integrated practice trials and instructions. A touch screen version does already exist (Stark Lab, 2013), but task format and presentation could be beneficial to examine further.

Future studies could also be aimed at measuring interindividual vulnerability and resiliency to sleep loss as this may also determine how individuals perform on cognitive tasks despite experiencing sleep debt. Indeed, research shows that proneness to performance deficits due to sleep loss might be associated with trait and biology (Van Dongen & Belenky, 2009; Mu et al., 2005). For example, individual differences in cognitive performance following sleep loss may be due to activation differences in prefrontal and parietal cortices, and genes (Goel et al., 2013; Satterfield et al., 2017; Dennis et al., 2017). It may also determine individual trajectories in terms of future cognitive decline, and targeting vulnerable individuals to sleep loss would perhaps be preventative of detrimental health outcomes. For example, neuroimaging could be implemented to measure brain activation before and after sleep deprivation during completion of CANTAB tests and tests of pattern separation. Such studies should take time-of-day or circadian effects upon cognitive performance into account. In addition, examining only the last night of sleep before cognitive testing the next day combined with self-reported sleep quality may also provide some insight into individual variability in how much sleep is needed. By examining these data, a difference score using the night before testing and the previous 6 days could aid the evaluation of whether the night before testing was sufficient for the individual. As individuals differ in terms of how much sleep they need in order to perform well on cognitive tests, this approach may be useful in studies that include more than one night of sleep. The approach could also be helpful in determining whether the last day of sufficient sleep quality and quantity provided recovery of function if the other days prior to testing included poor sleep.

To summarize, the cognitive measures that seem most sensitive to sleep are measures of pattern separation. Our results indicated that both the MST and the CANTAB DMS were sensitive to both sleep quantity (i.e., total sleep time) and sleep quality (i.e., sleep efficiency and WASO). We recommend that future studies aiming to identify individuals who may have cognitive impairment that could be alleviated with sleep-targeting therapeutics or clinical trials of sleep promoting interventions, use measures that tax pattern separation performance as a clinical outcome measure.

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Appendix A.

Scripts

PVT script

Please start the PVT at a time that is free from distractions. If distractions occur, then please report the number of distractions within the application when prompted following the test.

Hold the device in a landscape position each time and hover each of your thumbs over the device within a few millimeters of the screen the entire time you are taking this test (physically demonstrate).

During the test, tap the screen using the thumb of your dominant hand, that is, the hand you typically write with, as soon as you see red numbers scrolling in a box on the screen.

You must use the thumb of your dominant hand to respond to the stimuli in all tests. The numbers in the display show you how fast you responded each time – the smaller the number, the better you did.

Try to do your best and get the lowest number you possibly can each time. If you tap on the screen too early (before the numbers appear) you will see an error message, “FS”, indicating a false start. If you tap using your non-dominant thumb, then you will see the error message “ERR”, indicating an error. Avoid “FS” and “ERR”.

Do you have any questions?

MST Phase 1 script:

I want you to look at some pictures. When the computer program starts, it will show you pictures on the screen one by one. For each picture that you see, I want you to decide whether the item you see is an indoor item or an outdoor item. There is a little cue card below your screen to remind you what buttons to push. If you see an indoor item, I want you to press the V key on the keyboard. If you see an outdoor item, I want you to press the N key.

If you are not sure whether the item is an indoor item or an outdoor item, go ahead and take a guess, but try not to skip that trial. Also, the pictures are only on the screen for about two seconds. Try to get your responses in before the next picture comes up on the screen. Th computer will not indicate whether you are right or wrong.

Do you have any questions?

MST phase 2 script:

This second part will be a memory test for the items you just saw. I've flipped your cue card around, so you have a different set of responses to make. The computer will show you pictures on the screen again, one at a time. This time, however, for each picture, I want you to decide whether the picture is old, similar, or new.

So, if you see a picture on the screen, and it is the exact same picture as one you just saw in the previous phase, then I want you to press the V key for old, saying that is an old picture. If you see a new picture – it is new, it is different, and you have not seen it before – then I want you to press N for new. If you see a similar picture, which means, the picture comes up on the screen and you should be able to think something along the lines of, "oh, that is very similar to an old picture, but it is not the exact same picture", then I want you to press the B key for similar.

Do you have any questions?

Appendix B.

Tables

Table B.1. Sample characteristics for the correlational study

	Older adults		Younger adults	
	Total	%	Total	%
Sex				
Female	18	52.94 %	48	60.76 %
Male	16	47.06 %	31	39.24 %
Ethnicity				
First nations	1	2.94 %	0	0 %
Black	0	0 %	2	2.53 %
Black (Nigerian)	0	0 %	1	1.27 %
Hispanic	0	0 %	2	2.53 %
Caribbean	0	0 %	1	1.27 %
Pakistani	0	0 %	1	1.27 %
Indian	0	0 %	14	17.72 %
Indian-white	1	2.94 %	1	1.27 %
Asian	3	8.82 %	27	34.18 %
Asian-white	0	0 %	3	3.80 %
White	29	85.29 %	18	22.79 %
Medical history				
Mental health disorder				
Anxiety	2	5.88 %	6	7.59 %

Attention deficit disorder	0	0 %	3	3.80 %
Depression	5	14.71 %	1	1.27%
Depression and anxiety	2	5.88 %	4	5.06 %
PTSD	1	2.94 %	0	0 %
Neurological health				
Concussion	2	5.88 %	3	3.80 %
Brain surgery	1	2.94 %	0	0 %
Migraine	1	2.94 %	0	0 %
Dysautonomia	0	0 %	1	1.27 %
Sleep disorder				
Sleep apnea	4	11.77 %	0	0 %
Insomnia and sleep apnea	2	5.88 %	0	0 %
Insomnia	0	0 %	1	1.27 %
Insomnia and narcolepsy	0	0 %	1	1.27 %
Parasomnia	0	0 %	1	1.27 %
AD family history				
Yes	6	17.65 %	-	-
No	22	64.71 %	-	-
Not sure	6	17.65 %	-	-
Other health conditions				
Long haul covid	1	2.94 %	0	0 %
Diabetes	2	5.88 %	0	0 %

High blood pressure	4	11.77 %	0	0 %
Osteoporosis	1	2.94 %	0	0 %

Table B.2. Sleep parameters for the younger and older adults

Participants	TST (Hours)		SOL (Min)		SE (%)		WASO (Min)	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Older adults (N = 34)	7.19	.55	4.00	2.00	91.69	3.76	34.00	17.00
Younger adults (N = 79)	6.44	.50	4.00	2.00	91.60	4.74	28.00	20.00

Note. Means and standard deviations are displayed in clock time. TST = total sleep time; SOL = sleep onset latency; SE = sleep efficiency; WASO = wake after sleep onset.

Table B.3. Correlations between PVT outcomes and sleep parameters

PVT Outcomes	N	Sleep parameters							
		TST		SOL		SE		WASO	
		r/ρ	*p*	*r/ρ*	*p*	*r/ρ*	*p*	*r/ρ*	*p*
Younger adults									
Total lapses	76	ρ = .03	.80	ρ = .01	.91	ρ = -.08	.48	ρ = .11	.35
10% Fastest RT	76	*r* = .06	.62	ρ = -.03	.78	ρ = -.09	.44	ρ = .09	.43
10% Slowest RT	76	ρ = .01	.91	ρ = .04	.68	ρ = -.20	.08	ρ = .24	.04*
Mean 1/RT	76	*r* = -.001	.99	ρ = .004	.97	ρ = .13	.26	ρ = -.15	.21
Cognitive slowing	76	*r* = .06	.63	ρ = -.08	.52	ρ = .22	.06	ρ = -.24	.04*
Older adults									
Total lapses	29	ρ = -.14	.48	ρ = -.07	.71	ρ = -.15	.45	ρ = .10	.63
10% Fastest RT	29	*r* = -.30	.12	ρ = -.18	.34	*r* = -.04	.85	*r* = -.02	.91
10% Slowest RT	29	*r* = -.39	.04*	ρ = .07	.74	*r* = -.43	.02*	*r* = .36	.054
Mean 1/RT	29	*r* = .34	.07	ρ = .005	.98	*r* = .26	.17	*r* = -.20	.30

Cognitive slowing	29	*r* = .36	.054	*ρ* = -.07	.70	*r* = .39	04*	*r* = -.33	.08

Note. TST = total sleep time; SOL = sleep onset latency; SE= sleep efficiency; WASO = wake after sleep onset. Correlations with non-normal data were conducted using Spearman's rank correlation (*ρ*).

Table B.4. Correlations between MST outcomes and sleep parameters

MST Outcomes	N	Sleep parameters							
		TST		SOL		SE		WASO	
		r/ρ	*p*	*r/ρ*	*p*	*r/ρ*	*p*	*r/ρ*	*p*
Younger adults									
LDI	69	*r* = -.01	.92	*ρ* = .02	.87	*ρ* = .14	.26	*ρ* = -.19	.13
REC	69	*ρ* = .13	.30	*ρ* = .11	.39	*ρ* = -.03	.83	*ρ* = .0002	1.00
L1	69	*r* = .03	.84	*ρ* = .09	.44	*ρ* = .11	.35	*ρ* = -.14	.26
L2	69	*r* = .11	.38	*ρ* = .16	.20	*ρ* = -.02	.85	*ρ* = .001	1.00
L3	69	*r* = -.02	.89	*ρ* = .05	.70	*ρ* = .04	.76	*ρ* = -.09	.44
L4	69	*r* = -.07	.58	*ρ* = -.06	.63	*ρ* = .13	.29	*ρ* = -.18	.15
L5	69	*r* = -.09	.47	*ρ* = -.12	.34	*ρ* = .22	.07	*ρ* = -.24	.052
Older adults									
LDI	22	*ρ* = .28	.21	*ρ* = -.20	.37	*ρ* = .01	.98	*ρ* = -.06	.79
REC	22	*r* = -.20	.36	*ρ* = .04	.87	*r* = -.29	.20	*r* = .25	.25
L1	22	*r* = .40	.06	*ρ* = -.13	.56	*r* = .18	.43	*r* = -.07	.75
L2	22	*r* = .05	.82	*ρ* = -.16	.47	*r* = .06	.79	*r* = -.04	.88
L3	22	*r* = .20	.38	*ρ* = -.19	.40	*r* = .18	.44	*r* = -.16	.47
L4	22	*r* = .19	.39	*ρ* = -.20	.37	*r* = .14	.52	*r* = -.11	.63

L5	22	*r* = .12	.59	*ρ* = -.18	.42	*r* = .14	.55	*r* = -.10	.65

Note. TST = total sleep time; SOL = sleep onset latency; SE= sleep efficiency; WASO = wake after sleep onset; LDI= Lure Discrimination Index;REC= Recognition memory; L1 = Lure bin 1; L2 = Lure bin 2; L3 = Lure bin 3; L4 = Lure bin 4; L5 = Lure bin 5. Correlations with non-normal data were conducted using Spearman's rank correlation (*ρ*).

Table B.5. Correlations between CANTAB outcomes and sleep parameters

		Sleep parameters							
		TST		SOL		SE		WASO	
CANTAB Outcomes	N	*r/ρ*	*p*	*r/ρ*	*p*	*r/ρ*	*p*	*r/ρ*	*p*
Younger adults									
DMS									
DMSML	73	*ρ* = .07	.54	*ρ* = .06	.62	*ρ* = .15	.20	*ρ* = -.13	.27
DMSML0	73	*ρ* = .08	.51	*ρ* = .09	.46	*ρ* = .14	.24	*ρ* = -.13	.27
DMSML12	73	*ρ* = -.001	1.00	*ρ* = -.03	.77	*ρ* = .18	.13	*ρ* = -.16	.19
DMSML4	73	*ρ* = .13	.27	*ρ* = .05	.70	*ρ* = .04	.72	*ρ* = -.02	.88
DMSMLAD	73	*ρ* = .08	.47	*ρ* = .05	.65	*ρ* = .12	.29	*ρ* = -.10	.39
DMSMLS	73	*ρ* = .05	.70	*ρ* = .07	.58	*ρ* = .13	.29	*ρ* = -.10	.38
PAL									
PALFAMS	73	*ρ* = -.11	.36	*ρ* = -.16	.19	*ρ* = .04	.75	*ρ* = -.06	.64
PALMETS	73	*ρ* = .07	.54	*ρ* = .17	.15	*ρ* = -.13	.26	*ρ* = .14	.23
PALTEA	73	*ρ* = .10	.41	*ρ* = .13	.26	*ρ* = -.05	.65	*ρ* = .08	.48
PALTEA2	73	-	-	-	-	-	-	-	-
PALTEA4	73	*ρ*= -.05	.68	*ρ* = .01	.96	*ρ* = -.02	.87	*ρ* = .03	.83
PALTEA6	73	*ρ*= .09	.45	*ρ* = .11	.37	*ρ* = .11	.34	*ρ* = -.11	.36

PALTEA8	73	ρ = .08	.49	ρ = .13	.28	ρ = -.14	.23	ρ = .18	.14
5-Choice RTI									
RTIFMMT	73	ρ = .02	.85	ρ = -.21	.07	ρ = .11	.36	ρ = -.02	.86
SWM									
SWMBE	73	ρ = -.04	.77	ρ = .06	.64	ρ = -.13	.26	ρ = .17	.15
SWMBE4	73	ρ = .10	.42	ρ = .13	.28	ρ = -.12	.31	ρ = .17	.14
SWMBE6	73	ρ = -.02	.86	ρ = .12	.30	ρ = -.24	.04*	ρ = .27	.02*
SWMBE8	73	ρ = -.05	.68	ρ = .04	.71	ρ = -.10	.39	ρ = .14	.25
SWMS	73	ρ = -.03	.81	ρ = .08	.52	ρ = -.05	.67	ρ = .05	.70
Older adults									
DMS									
DMSML	34	r = .03	.87	ρ = .01	.95	r = -.17	.35	r = .21	.24
DMSML0	33	r = .03	.87	ρ = .02	.91	r = -.01	.97	r = .02	.91
DMSML12	34	ρ = .02	.90	ρ = .07	.67	ρ = -.20	.26	ρ = .24	.17
DMSML4	34	r = -.13	.46	ρ = -.002	.99	r = -.37	.03*	r = .39	.02*
DMSMLAD	34	r = -.02	.94	ρ = .05	.76	r = -.23	.18	r = .27	.12
DMSMLS	34	ρ = .14	.43	ρ = -.01	.93	ρ = .04	.82	ρ = .02	.89
PAL									
PALFAMS	34	r = .08	.65	ρ = .14	.44	r = .15	.40	r = -.16	.37
PALMETS	34	ρ = .03	.89	ρ = .03	.89	ρ = .12	.51	ρ = -.12	.50
PALTEA	34	ρ = .04	.82	ρ = -.15	.40	ρ = -.07	.67	ρ = .10	.57
PALTEA2	34	ρ = .17	.32	ρ = .07	.71	ρ = -.20	.27	ρ = .31	.07

PALTEA4	34	ρ = -.09	.63	ρ = -.17	.33	ρ = -.22	.20	ρ = .24	.17
PALTEA6	34	ρ = .02	.93	ρ = -.30	.09	ρ = -.11	.55	ρ = .17	.34
PALTEA8	34	ρ = .09	.62	ρ = -.06	.75	ρ = -.08	.67	ρ = .11	.54
5-Choice RTI									
RTIFMMT	34	ρ = -.13	.48	ρ = -.11	.55	ρ = .16	.36	ρ = -.16	.37
SWM									
SWMBE	34	ρ = -.08	.64	ρ = -.22	.21	ρ = -.19	.28	ρ = .19	.28
SWMBE4	34	ρ = -.25	.16	ρ = -.29	.09	ρ = .01	.96	ρ = -.05	.76
SWMBE6	34	ρ = -.07	.70	ρ = -.26	.13	ρ = -.10	.59	ρ = .10	.57
SWMBE8	34	ρ = -.01	.95	ρ = -.07	.68	ρ = -.27	.12	ρ = .30	.09
SWMS	34	ρ = -.13	.45	ρ = .02	.90	ρ = -.08	.64	ρ = .04	.83

Note. TST = total sleep time; SOL = sleep onset latency; SE= sleep efficiency; WASO = wake after sleep onset; DMSML = DMS Mean Correct Latency; DMSML0 = DMS Mean Correct Latency (0 s delay); DMSML12 = DMS Mean Correct Latency (12 s delay); DMSML4 = DMS Mean Correct Latency (4 s delay); DMSMLAD = DMS Mean Correct Latency (All Delays); DMSMLS = DMS Mean Latency Simultaneous; PALFAMS = PAL First Attempt Memory Score; PALMETS = PAL Mean Errors to Success; PALTEA = PAL Total Errors (Adjusted); PALTEA2 = PAL Total Errors 2 Shapes (Adjusted); PALTEA4= PAL Total Errors 4 Shapes (Adjusted); PALTEA6 = PAL Total Errors 6 Shapes (Adjusted); PALTEA8 = PAL Total Errors 8 Shapes (Adjusted); RTIFMMT = RTI Mean Five-Choice Movement Time; SWMBE = SWM Between Errors; SWMBE4 = SWM Between errors 4 boxes; SWMBE6 = SWM Between errors 6 boxes; SWMBE8 = SWM Between errors 8 boxes; SWMS = SWM Strategy (6-8 boxes). Correlations with non-normal data were conducted using Spearman's rank correlation (ρ).

Table B.6. Correlations between CANTAB outcomes and the Montreal Cognitive Assessment

CANTAB outcomes	N	M	SD	*r*/ρ	*p*
DMS					
DMSML	34	3550	933.10	*r* = -.007	.97
DMSML0	33	3194	924.60	*r* = .30	.09
DMSML12	34	4273	1601	ρ = -.10	.59
DMSML4	34	3720	1037	*r* = -.05	.76

DMSMLAD	34	3706	978.70	r = .05	.78
DMSMLS	34	3165	1011	ρ = -.09	.62
PAL					
PALFAMS	34	11.24	4.43	r = .55	<.001***
PALMETS	34	1.82	1.36	ρ = -.14	.43
PALTEA	34	21.35	16.05	ρ = -.45	.01*
PALTEA2	34	.12	.41	ρ = -.15	.40
PALTEA4	34	1.56	2.43	ρ = -.40	.02*
PALTEA6	34	5.47	5.89	ρ = -.54	<.001***
PALTEA8	34	14.21	9.80	ρ = -.30	.08
5-Choice RTI					
RTIFMMT	34	275.00	67.36	ρ = -.07	.68
SWM					
SWMBE	34	16.32	7.60	ρ = -.59	<.001***
SWMBE4	34	1.06	1.15	ρ = -.45	.01*
SWMBE6	34	4.24	3.12	ρ = -.50	.003**
SWMBE8	34	11.03	5.11	ρ = -.45	.01*
SWMS	34	8.88	2.10	ρ = -.35	.04*

Note. DMSML = DMS Mean Correct Latency; DMSML0 = DMS Mean Correct Latency (0 s delay); DMSML12 = DMS Mean Correct Latency (12 s delay); DMSML4 = DMS Mean Correct Latency (4 s delay); DMSMLAD = DMS Mean Correct Latency (All Delays); DMSMLS = DMS Mean Latency Simultaneous; PALFAMS = PAL First Attempt Memory Score; PALMETS = PAL Mean Errors to Success; PALTEA = PAL Total Errors (Adjusted); PALTEA2 = PAL Total Errors 2 Shapes (Adjusted); PALTEA4 = PAL Total Errors 4 Shapes (Adjusted); PALTEA6 = PAL Total Errors 6 Shapes (Adjusted); PALTEA8 = PAL Total Errors 8 Shapes (Adjusted); RTIFMMT = RTI Mean Five-Choice Movement Time; SWMBE = SWM Between Errors; SWMBE4 = SWM Between Errors 4 boxes; SWMBE6 = SWM Between Errors 6 boxes; SWMBE8 = SWM Between Errors 8 boxes; SWMS = SWM Strategy (6-8 boxes). Correlations with non-normal data were conducted using Spearman's rank correlation (ρ).

Table B.7. Correlations between MST outcomes and Clocklab parameters

		Clocklab parameters							
MST Outcomes	N	Amplitude		Acrophase		IV		IS	
		r/ρ	*p*	*r/ρ*	*p*	*r/ρ*	*p*	*r/ρ*	*p*
Younger adults									
LDI	45	ρ = .28	.06	*r* = -.05	.76	*r* = -.21	.16	*r* = .09	.57
REC	45	ρ = -.07	.63	ρ = -.13	.39	ρ = .14	.37	ρ = -.14	.35
L1	45	ρ = .19	.22	*r* = -.12	.45	*r* = -.15	.33	*r* = .17	.27
L2	45	ρ = .36	.02*	*r* = .04	.79	*r* = -.17	.26	*r* = .11	.45
L3	45	ρ = .12	.43	*r* = -.09	.58	*r* = .05	.77	*r* = .06	.70
L4	45	ρ = .35	.02*	*r* = -.13	.38	*r* = -.41	.01*	*r* = .10	.50
L5	45	ρ = .06	.71	*r* = .08	.62	*r* = -.10	.51	*r* = -.13	.40
Older adults									
LDI	21	ρ = -.22	.32	ρ = .14	.54	ρ = .56	.01*	ρ = .01	.96
REC	21	*r* = .14	.55	*r* = .03	.91	*r* = -.06	.79	*r* = -.22	.34
L1	21	*r* = -.19	.41	*r* = -.10	.67	*r* = .48	.03*	*r* = -.05	.83
L2	21	*r* = -.18	.44	*r* = -.04	.87	*r* = .46	.04*	*r* = .23	.32
L3	21	*r* = -.14	.56	*r* = -.20	.38	*r* = .53	.01*	*r* = -.16	.49
L4	21	*r* = -.14	.54	*r* = -.11	.63	*r* = .56	.01*	*r* = -.10	.68
L5	21	*r* = -.24	.29	*r* = .07	.76	*r* = .61	.003**	*r* = .09	.70

Note. IV = Intradaily Variability; IS = Interdaily Stability; LDI = Lure Discrimination Index; REC= Recognition memory; L1 = Lure bin 1; L2 = Lure bin 2; L3 = Lure bin 3; L4 = Lure bin 4; L5 = Lure bin 5. Correlations with non-normal data were conducted using Spearman's rank correlation (ρ).

Table B.8. Correlations between CANTAB outcomes and Clocklab parameters

CANTAB Outcomes	N	Clocklab parameters: Amplitude		Acrophase		IV		IS	
		r/ρ	*p*	*r/ρ*	*p*	*r/ρ*	*p*	*r/ρ*	*p*
Younger adults									
DMS									
DMSML	45	ρ = -.09	.56	ρ = .26	.08	ρ = .09	.54	ρ = -.10	.51
DMSML0	45	ρ = -.02	.90	ρ = .32	.03*	ρ = .10	.50	ρ = -.05	.72
DMSML12	45	ρ = -.17	.26	ρ = .25	.11	ρ = .10	.53	ρ = -.04	.78
DMSML4	45	ρ = .10	.52	ρ = .24	.12	ρ = -.05	.73	ρ = -.09	.56
DMSMLAD	45	ρ = -.05	.74	ρ = .27	.08	ρ = .05	.72	ρ = -.08	.59
DMSMLS	45	ρ = -.01	.94	ρ = .19	.21	ρ = .12	.41	ρ = .02	.89
PAL									
PALFAMS	45	ρ = -.12	.42	ρ = .10	.52	ρ = -.02	.90	ρ = -.09	.55
PALMETS	45	ρ = .20	.20	ρ = -.01	.96	ρ = .003	.98	ρ = .09	.54
PALTEA	45	ρ = .11	.49	ρ = -.08	.59	ρ = .06	.72	ρ = .07	.63
PALTEA2	45	-	-	-	-	-	-	-	-
PALTEA4	45	ρ = -.08	.61	ρ = -.09	.54	ρ = -.07	.63	ρ = .06	.69
PALTEA6	45	ρ = .21	.16	ρ = -.17	.26	ρ = -.09	.55	ρ = .18	.25
PALTEA8	45	ρ = .06	.68	ρ = .01	.94	ρ = .12	.42	ρ = -.01	.94
5-Choice RTI									
RTIFMMT	45	ρ = -.22	.15	*r* = .19	.20	*r* = .05	.75	*r* = -.20	.20
SWM									

SWMBE	45	ρ = .11	.46	ρ = -.16	.30	ρ = .23	.14	ρ = .09	.55
SWMBE4	45	ρ = .25	.10	ρ = -.15	.33	ρ = .01	.97	ρ = .17	.25
SWMBE6	45	ρ = .07	.64	ρ = -.16	.29	ρ = .20	.19	ρ = .11	.46
SWMBE8	45	ρ = .15	.31	ρ = -.15	.33	ρ = .18	.23	ρ = .08	.61
SWMS	45	ρ = .17	.25	ρ = -.08	.61	ρ = -.04	.80	ρ = .07	.64
Older adults									
DMS									
DMSML	33	*r* = -.03	.85	*r* = .05	.79	*r* = -.02	.93	*r* = .09	.61
DMSML0	32	*r* = .09	.63	*r* = -.19	.29	*r* = -.04	.83	*r* = .13	.49
DMSML12	33	ρ = .03	.85	ρ = .03	.86	ρ = -.04	.82	ρ = .15	.41
DMSML4	33	*r* = .16	.37	*r* = -.07	.70	*r* = -.11	.53	*r* = .12	.51
DMSMLAD	33	*r* = .05	.77	*r* = -.06	.74	*r* = -.06	.72	*r* = .11	.55
DMSMLS	33	ρ = -.29	.11	ρ = .12	.52	ρ = .21	.23	ρ = .03	.88
PAL									
PALFAMS	33	*r* = .13	.46	*r* = -.19	.29	*r* = -.06	.74	*r* = -.01	.97
PALMETS	33	ρ = -.03	.88	ρ = .16	.36	ρ = .10	.57	ρ = .05	.79
PALTEA	33	ρ = -.06	.74	ρ = -.03	.88	ρ = .11	.54	ρ = .06	.75
PALTEA2	33	ρ = -.05	.77	ρ = .14	.45	ρ = .17	.34	ρ = .06	.75
PALTEA4	33	ρ = .03	.88	ρ = .10	.59	ρ = .12	.52	ρ = .23	.21
PALTEA6	33	ρ = -.004	.98	ρ = -.05	.80	ρ = -.11	.54	ρ = .10	.60
PALTEA8	33	ρ = -.11	.56	ρ = -.02	.91	ρ = .22	.22	ρ = .01	.98
5-Choice RTI									

RTIFMMT	33	ρ = .05	.78	ρ = .24	.18	ρ = -.17	.34	ρ = .08	.65
SWM									
SWMBE	33	ρ = -.09	.63	ρ = -.02	.90	ρ = .01	.94	ρ = -.01	.96
SWMBE4	33	ρ = -.23	.21	ρ = .37	.04*	ρ = .17	.33	ρ = -.15	.41
SWMBE6	33	ρ = .01	.97	ρ = -.05	.78	ρ = -.17	.34	ρ = .11	.53
SWMBE8	33	ρ = -.12	.50	ρ = -.06	.74	ρ = .03	.88	ρ = -.12	.49
SWMS	33	ρ = .01	.95	ρ = -.20	.26	ρ = -.16	.38	ρ = .22	.21

Note. IV = intradaily variability; IS = interdaily stability; DMSML = DMS Mean Correct Latency; DMSML0 = DMS Mean Correct Latency (0 s delay); DMSML12 = DMS Mean Correct Latency (12 s delay); DMSML4 = DMS Mean Correct Latency (4 s delay); DMSMLAD = DMS Mean Correct Latency (All Delays); DMSMLS = DMS Mean Latency Simultaneous; PALFAMS = PAL First Attempt Memory Score; PALMETS = PAL Mean Errors to Success; PALTEA = PAL Total Errors (Adjusted); PALTEA2 = PAL Total Errors 2 Shapes (Adjusted); PALTEA4 = PAL Total Errors 4 Shapes (Adjusted); PALTEA6 = PAL Total Errors 6 Shapes (Adjusted); PALTEA8 = PAL Total Errors 8 Shapes (Adjusted); RTIFMMT = RTI Mean Five-Choice Movement Time; SWMBE = SWM Between Errors; SWMBE4 = SWM Between Errors 4 boxes; SWMBE6 = SWM Between Errors 6 boxes; SWMBE8 = SWM Between Errors 8 boxes; SWMS = SWM Strategy (6-8 boxes). Correlations with non-normal data were conducted using Spearman's rank correlation (ρ).

Table B.9. Sex comparison on sleep quantity and quality in the younger adults

	YA females	YA males				
	N = 48	N = 31				
Sleep parameters	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI
TST	6.93 ± .11	6.47 ± .15	t-test	t(77) = 2.45	.02	-0.82, -0.09
SOL	.07 (.03-.08)	.07 (.05-.10)	MWU	U = 695	.62	-
SE	92.32 (89.47 - 95.40)	92.68 (90.36 - 94.10)	MWU	U = 701.5	.67	-
WASO	.43 (.25 - .70)	.42 (.27 - .53)	MWU	U = 736.5	.94	-

Note. Data are shown as median (interquartile range [IQR]) or mean ± standard deviation (SD). Data are displayed in decimal time. TST = total sleep time; SOL = sleep onset latency; SE = sleep efficiency; WASO = wake after sleep onset.

Table B.10. Sex comparison on sleep quantity and quality in the older adults

	OA females	OA males				
	N = 18	N = 16				
Sleep parameters	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI

TST	7.49 (6.75 – 8.19)	7.29 (7.02 – 7.89)	MWU	U = 125	.52	-
SOL	.07 (.03 - .07)	.07 (.04 - .10)	MWU	U = 114.5	.31	-
SE	91.74 ± .98	91.64 ± .84	t-test	t(32) = 0.07	.94	-2.76, 2.58
WASO	.57 ± .07	.56 ± .07	t-test	t(32) = 0.08	.94	-0.22, 0.20

Note. Data are shown as median (interquartile range [IQR]) or mean ± standard deviation (SD). Data are displayed in decimal time. TST = total sleep time; SOL = sleep onset latency; SE = sleep efficiency; WASO = wake after sleep onset.

Table B.11. Comparison of older and younger adults' MST performance

	YA	OA					
	N = 69	N = 22					Effect size
MST outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI	Cohen's D/ r_{rb}
LDI	.40 (.28-.51)	.27 (.15-.41)	MWU	U = 471	.007**	-	.38
REC	. 84 (.77-.89)	.81 (.70-.86)	MWU	U = 573	.09	-	
L1	.21 ± .02	.16 ± .04	t-test	t(89) = 1.33	.19	-.13, .03	
L2	.31 ± .02	.22 ± .05	t-test	t(89) = 1.85	.07	-.19, .01	
L3	.42 ± .02	.35 ± .05	t-test	t(89) = 1.29	.20	-.17, .04	
L4	.52 ± .02	.36 ± .06	t-test	t(27.05) = 2.47	.02	-.30, -.03	
L5	.54 ± .02	.39 ± .05	t-test	t(27.28) = 2.55	.02	-.27, -.03	

Note. MWU = Mann -Whitney U test; t-test = independent t-test; SEM = standard error of the mean; MD= median; IQR = interquartile range; YA = younger adults; OA= older adults; r_{rb} = Rank- Biserial correlation (r); LDI = Lure Discrimination Index; REC= Recognition memory; L1 = Lure bin 1; L2 = Lure bin 2; L3 = Lure bin 3; L4 = Lure bin 4; L5 = Lure bin 5. Significant at *p* = .007** (Bonferroni)

Table B.12. Comparison of the older and younger adults' CANTAB performance

	YA	OA			
	N = 73	N = 34			
	MD (IQR)	MD (IQR)	U	*p*	r_{rb}
DMS					
DMSML	2481 (2037 - 2963)	3497 (2930 - 4028)	519	<.001***	.21
DMSML0	2258 (1821 – 2836)	3041 (2466 – 3734)	598	<.001***	.24

DMSML4	2483 (2059 – 3160)	3703 (3083 – 4276)	530	<.001***	.21
DMSML12	2660 (2228 – 3605)	4050 (3242 -4637)	592	<.001***	.24
DMSMLAD	2568 (2033-3090)	3528 (3098-4290)	517	<.001***	.21
DMSMLS	2339 (1871 – 2826)	2989 (2541 – 3563)	627	<.001***	.25
PAL					
PALFAMS	18.00 (15.00 -19.00)	12.00 (7.75 – 15.00)	333.50	<.001***	.13
PALMETS	0.00 (0.00 – 1.50)	2.00 (1.00 – 2.00)	678.50	<.001***	.27
PALTEA	3.00 (1.00 – 6.00)	18.00 (8.00 – 36.50)	276.50	<.001***	.11
PALTEA2	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	1132	.03	
PALTEA4	0.00 (0.00 – 0.00)	0.00 (0.00 – 3.00)	805	<.001***	.32
PALTEA6	0.00 (0.00 – 2.00)	3.00 (0.00 – 11.00)	617	<.001***	.25
PALTEA8	2.00 (0.00 – 4.00)	11.50 (5.75 – 28.00)	305.5	<.001***	.12
5-Choice RTI					
RTIFMMT	219.80 (194.60 – 249.50)	252 (229.3 – 318.6)	652	<.001***	.26
SWM					
SWMBE	3.00 (0.00 – 13.00)	19.00 (11.75 – 22.00)	488.50	<.001***	.20
SWMBE4	0.00 (0.00 – 0.00)	0.50 (0.00 – 2.00)	789.50	<.001***	.32
SWMBE6	0.00 (0.00 – 3.00)	4.50 (1.75 – 7.00)	704	<.001***	.28
SWMBE8	0.00 (2.00 – 9.00)	12.50 (8.00 – 14.00)	507.50	<.001***	.21
SWMS	7.00 (5.00 – 9.00)	9.00 (8.00 – 9.00)	598.50	<.001***	.24

Note. YA= younger adults; OA= older adults, MD = median; IQR = Interquartile range; SEM = standard error of the mean; r_{rb} = Rank- Biserial correlation (r); DMSML = DMS Mean Correct Latency; DMSML0 = DMS Mean Correct Latency (0 s delay); DMSML12 = DMS Mean Correct Latency (12 s delay); DMSML4 = DMS Mean Correct Latency (4 s delay); DMSMLAD = DMS Mean Correct Latency (All Delays); DMSMLS = DMS Mean Latency Simultaneous; PALFAMS = PAL First Attempt Memory Score; PALMETS = PAL Mean Errors to Success; PALTEA = PAL Total Errors (Adjusted); PALTEA2 = PAL Total Errors 2 Shapes (Adjusted); PALTEA4 = PAL Total Errors 4 Shapes (Adjusted); PALTEA6 = PAL Total Errors 6 Shapes (Adjusted); PALTEA8 =

PAL Total Errors 8 Shapes (Adjusted); RTIFMMT = RTI Mean Five-Choice Movement Time; SWMBE = SWM Between Errors; SWMBE4 = SWM Between Errors 4 boxes; SWMBE6 =SWM Between Errors 6 boxes; SWMBE8 = SWM Between Errors 8 boxes; SWMS = SWM Strategy (6-8 boxes).
Significant at p = .003** (Bonferroni).

Table B.13. Sex comparison on the MST for the younger adults

	YA females	YA males				
	N = 45	N = 24				
MST outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI
LDI	.42 ± .02	.39 ± .03	t-test	t(67) = 0.77	.44	-.10, .05
REC	.85 (.79 - .89)	.81 (.72 - .87)	MWU	U = 411	.11	-
L1	.22 ± .02	.20 ± .04	t-test	t(67) = 0.49	.63	-.10, .06
L2	.33 ± .03	.28 ± .04	t-test	t(67) = 1.03	.31	-.16, .05
L3	.44 ± .04	.39 ± .04	t-test	t(67) = 0.99	.33	-.15, .05
L4	.53 ± .03	.51 ± .03	t-test	t(67) = 0.33	.75	-.11, .08
L5	.55 ± .03	.53 ± .03	t-test	t(67) = 0.32	.75	-.10, .07

Note. MWU = Mann- Whitney U test; t- test = independent t-test; YA = younger adults; MD = median; IQR = Interquartile range; SEM = standard error of the mean; LDI = Lure Discrimination Index; REC= Recognition memory; L1 = Lure bin 1; L2 = Lure bin 2; L3 = Lure bin 3; L4 =Lure bin 4; L5 = Lure bin 5.
Significant at p = .007** (Bonferroni)

Table B.14. Sex comparison on the MST for the older adults

	OA females	OA males				
	N = 10	N = 12				
MST outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI
LDI	.37 ± .09	.26 ± .04	t-test	t(20) = 1.23	.23	-.30, .08
REC	.76 ± .03	.80 ± .02	t-test	t(20) = 1.06	.30	-.04, .12
L1	.23 ± .07	.10 ± .03	t-test	t(20) = 1.84	.08	-.27, .02
L2	.29 ± .08	.16 ± .05	t-test	t(20) = 1.46	.16	-.32, .06

L3	.39 ± .08	.33 ± .06	t-test	t(20) = 0.58	.57	-.27, .15
L4	.30 (.18 - .75)	.31 (.06 - .58)	MWU	U = 46	.38	-
L5	.44 ± .10	.35 ± .06	t-test	t(20) = 0.83	.41	-.32, .14

Note. MWU = Mann- Whitney U test; t- test = independent t-test; OA = older adults; YA = younger adults; MD = median; IQR = Interquartile range; SEM = standard error of the mean; LDI = Lure Discrimination Index; REC= Recognition memory; L1 = Lure bin 1; L2 = Lure bin 2; L3 = Lure bin 3; L4 = Lure bin 4; L5 = Lure bin 5.
Significant at p = .007** (Bonferroni)

Table B.15. Sex comparison on the CANTAB for the older adults

	OA females	OA males				
	N = 18	N = 16				
CANTAB outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	p	95% CI
DMS						
DMSML	3475 (2720 -4249)	3512 (3038 – 3724)	MWU	U = 128	.60	-
DMSML0	3103 ± 200.20	3290 ± 259.50	t-test	t(31) = .57	.57	-476.9, 850.7
DMSML4	3644 ± 280.10	3805 ± 216.80	t-test	t(32) = .44	.66	-574.8, 895.2
DMSML12	3860 (2893 - 4645)	4115 (3341 - 4940)	MWU	U = 118	.38	-
DMSMLAD	3504 (2766 - 4474)	3600 (3137 - 4250)	MWU	U = 134	.75	-
DMSMLS	2902 (2473 - 3493)	3021 (2518 - 4130)	MWU	U = 122	.46	-
PAL						
PALFAMS	11.39 ± 1.08	11.06 ± 1.10	t-test	t(32) = .21	.83	-3.47, 2.82
PALMETS	2.00 (1.00 – 2.00)	2.00 (1.00 – 2.00)	MWU	U = 143.5	.99	-
PALTEA	19.50 (8.75 – 36.50)	17.00 (7.25 - 35.50)	MWU	U = 136	.79	-
PALTEA2	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	MWU	U = 120	.23	-
PALTEA4	1.00 (0.00 – 4.00)	0.00 (0.00 – 2.75)	MWU	U = 107	.17	-
PALTEA6	3.00 (1.50 – 10.25)	3.00 (0.00 – 11.75)	MWU	U = 132	.68	-

PALTEA8	11.50 (6.00 – 28.00)	11.50 (5.25 – 25.50)	MWU	U = 143.5	.99	-
5-Choice RTI						
RTIFMMT	277.60 ± 17.22	272.10 ± 15.64	t-test	t(32) = .24	.81	-53.38, 42.28
SWM						
SWMBE	16.50 ± 1.84	16.13 ± 1.90	t-test	t(32) = .14	.89	-5.77, 5.02
SWMBE4	0.50 (0.00 – 2.00)	1.00 (0.00 – 2.00)	MWU	U = 137	.86	-
SWMBE6	4.56 ± 0.68	3.88 ± 0.85	t-test	t(32) = .63	.53	-2.88, 1.52
SWMBE8	12.50 (7.70 – 14.50)	12.50 (9.75 – 14.00)	MWU	U = 142	.95	-
SWMS	8.89 ± 0.45	8.88 ± 0.59	t-test	t(32) = .02	.99	-1.51, 1.48

Note. MWU = Mann- Whitney U test; t- test = independent t-test; OA= older adults, MD = median; IQR = interquartile range; SEM = standard error of the mean; DMSML = DMS Mean Correct Latency; DMSML0 = DMS Mean Correct Latency (0 s delay); DMSML12 = DMS Mean Correct Latency (12 s delay); DMSML4 = DMS Mean Correct Latency (4 s delay); DMSMLAD = DMS Mean Correct Latency (All Delays); DMSMLS = DMS Mean Latency Simultaneous; PALFAMS = PAL First Attempt Memory Score; PALMETS = PAL Mean Errors to Success; PALTEA = PAL Total Errors (Adjusted); PALTEA2 = PAL Total Errors 2 Shapes (Adjusted); PALTEA4 = PAL Total Errors 4 Shapes (Adjusted); PALTEA6 = PAL Total Errors 6 Shapes (Adjusted); PALTEA8 = PAL Total Errors 8 Shapes (Adjusted); RTIFMMT = RTI Mean Five-Choice Movement Time; SWMBE = SWM Between Errors; SWMBE4 = SWM Between Errors 4 boxes; SWMBE6 = SWM Between Errors 6 boxes; SWMBE8 = SWM Between Errors 8 boxes; SWMS = SWM Strategy (6-8 boxes).
Significant at p = .003** (Bonferroni)

Table B.16. Sex comparison on the CANTAB for the younger adults

	YA females	YA males				
	N = 44	N = 29				
CANTAB outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	p	95% CI
DMS						
DMSML	2342 (2002 – 2866)	2742 (2076 – 3202)	MWU	U = 529.50	.22	-
DMSML0	2189 (1789 – 2756)	2325 (1908 – 3044)	MWU	U = 528.50	.22	-
DMSML4	2391 (2027 – 2940)	2589 (2156 - 3280)	MWU	U = 564.50	.41	-
DMSML12	2555 (2250 – 3502)	3010 (2175 – 3705)	MWU	U = 599.50	.67	-

DMSMLAD	2505 (2032 – 2917)	2747 (2028 – 3298)	MWU	U = 556.50	.36	-
DMSMLS	2203 (1778 – 2574)	2572 (1968 – 3149)	MWU	U = 469.50	.06	-
PAL						
PALFAMS	18.00 (16.00 – 19.00)	16.00 (14.00 - 19.00)	MWU	U = 505	.13	-
PALMETS	0.00 (0.00 – 1.00)	1.00 (0.00 – 2.00)	MWU	U = 554	.31	-
PALTEA	2.00 (1.00 – 5.75)	4.00 (1.00 – 9.00)	MWU	U = 515.50	.17	-
PALTEA2	-	-	-	-	-	-
PALTEA4	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	MWU	U = 580.50	.29	-
PALTEA6	0.00 (0.00 – 1.75)	0.00 (0.00 – 2.50)	MWU	U = 532	.17	-
PALTEA8	2.00 (0.00 – 4.00)	2.00 (0.00 – 4.50)	MWU	U = 557.50	.36	-
5-Choice RTI						
RTIFMMT	220.90 ± 7.21	226.1 ± 9.49	t-test	t(71) = .44	.66	-18.26, 28.60
SWM						
SWMBE	6.00 (0.00 – 12.75)	2.00 (0.00 – 12.50)	MWU	U = 593	.61	-
SWMBE4	0.00 (0.00 – 0.00)	0.00 (0.00 – .00)	MWU	U = 590	.43	-
SWMBE6	0.00 (0.00 – 3.00)	0.00 (0.00 – 4.00)	MWU	U = 612	.75	-
SWMBE8	3.50 (0.00 – 9.50)	1.00 (0.00 – 7.50	MWU	U = 559.50	.36	-
SWMS	7.00 (5.25 – 9.00)	7.00 (4.00 – 7.50)	MWU	U = 530	.22	-

Note. MWU = Mann- Whitney U test; t- test = independent t-test; YA= younger adults; MD = median; IQR = interquartile range; SEM = standard error of the mean; DMSML = DMS Mean Correct Latency; DMSML0 = DMS Mean Correct Latency (0 s delay); DMSML12 = DMS Mean Correct Latency (12 s delay); DMSML4 = DMS Mean Correct Latency (4 s delay); DMSMLAD = DMS Mean Correct Latency (All Delays); DMSMLS = DMS Mean Latency Simultaneous; PALFAMS = PAL First Attempt Memory Score; PALMETS = PAL Mean Errors to Success; PALTEA = PAL Total Errors (Adjusted); PALTEA2 = PAL Total Errors 2 Shapes (Adjusted); PALTEA4 = PAL Total Errors 4 Shapes (Adjusted); PALTEA6 = PAL Total Errors 6 Shapes (Adjusted); PALTEA8 = PAL Total Errors 8 Shapes (Adjusted); RTIFMMT = RTI Mean Five-Choice Movement Time; SWMBE = SWM Between Errors; SWMBE4 = SWM Between Errors 4 boxes; SWMBE6 = SWM Between Errors 6 boxes; SWMBE8 = SWM Between Errors 8 boxes; SWMS = SWM Strategy (6-8 boxes).
Significant at $p = .003$** (Bonferroni)

Table B.17. Comparison of MST performance between good and bad sleepers (TST) in the younger adult sample

	YA good sleepers	YA bad sleepers				
	N = 17	N = 17				
MST outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI
LDI	.39 ± .04	.39 ± .04	t-test	t(32) = .07	.94	-.10, .11
REC	.82 ± .03	.80 ± .02	t-test	t(32) = .59	.56	-.09, .05
L1	.22 (.13 - .33)	.19 (.12 - .22)	MWU	U = 118.50	.38	-
L2	.31 ± .05	.27 ± .05	t-test	t(32) = .59	.56	-.18, .10
L3	.40 ± .05	.43 ± .05	t-test	t(32) = .49	.63	-.12, .19
L4	.49 ± .05	.50 ± .04	t-test	t(32) = .24	.81	-.12, .16
L5	.50 ± .05	.53 ± .04	t-test	t(32) = .48	.63	-.10, .17

Note. MWU = Mann- Whitney U test; t- test = independent t-test; YA= younger adults; MD = median; IQR = interquartile range; SEM = standard error of the mean; LDI = Lure Discrimination Index; REC= Recognition memory; L1 = Lure bin 1; L2 = Lure bin 2; L3 = Lure bin 3; L4 = Lure bin 4; L5 = Lure bin 5.
Significant at $p = .007$** (Bonferroni)

Table B.18. Comparison of MST performance between good and bad sleepers (sleep efficiency) in the younger adult sample

	YA good sleepers	YA bad sleepers				
	N = 16	N = 18	Independent t-test			
MST outcomes	Mean ± SEM	Mean ± SEM	df	t	*p*	95% CI
LDI	.43 ± .02	.39 ± .03	32	1.44	.16	-.17, .03
REC	.83 ± .01	.80 ± .02	32	.94	.35	-.10, .04
L1	.22 ± .02	.20 ± .04	32	1.02	.32	-.16, .05
L2	.33 ± .03	.28 ± .04	32	.38	.71	-.18, .12
L3	.44 ± .03	.39 ± .04	32	.21	.84	-.16, .13
L4	.53 ± .03	.51 ± .03	32	1.51	.14	-.24, .04
L5	.55 ± .03	.53 ± .03	32	2.37	.02	-.25, -.02

Note. YA= younger adults; MD = median; IQR = interquartile range; SEM = standard error of the mean; LDI = Lure Discrimination Index; REC= Recognition memory; L1 = Lure bin 1; L2 = Lure bin 2; L3 = Lure bin 3; L4 = Lure bin 4; L5 = Lure bin 5.
Significant at p = .007 (Bonferroni)

Table B.19. Comparison of MST performance between good and bad sleepers (TST) in the older adult sample

	OA good sleepers	OA bad sleepers				
	N = 8	N = 4				
MST outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI
LDI	.40 ± .10	.29 ± .11	t-test	t(10) = .70	.50	-.49, .25
REC	.70 (.66 - .82)	.82 (.67 - .82)	MWU	U = 14	.81	-
L1	.24 ± .08	.08 ± .04	t-test	t(10) = 1.29	.23	-.44, .12
L2	.26 ± .12	.27 ± .08	t-test	t(10) = .01	.99	-.40, .40
L3	.49 ± .06	.36 ± .17	t-test	t(10) = .88	.40	-.46, .20
L4	.44 ± .13	.35 ± .14	t-test	t(10) = .43	.68	-.56, .38
L5	.48 ± .12	.38 ± .13	t-test	t(10) = .53	.61	-.54, .33

Note. YA= younger adults; MD = median; IQR = interquartile range; SEM = standard error of the mean; LDI = Lure Discrimination Index; REC= Recognition memory; L1 = Lure bin 1; L2 = Lure bin 2; L3 = Lure bin 3; L4 = Lure bin 4; L5 = Lure bin 5.
Significant at p = .007 (Bonferroni)

Table B.20. Comparison of CANTAB performance between good and bad sleepers (TST) in the younger adult sample

	YA good sleepers	YA bad sleepers				
	N = 18	N = 18				
CANTAB outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI
DMS						
DMSML	2588 ± 150.40	2469 ± 169.40	t-test	t(34) = .53	.60	-579.30, 341.30
DMSML0	2342 (1977 – 2821)	2085 (1758 – 2906)	MWU	U = 142	.54	-

DMSML4	2368 (1934 – 3241)	2291 (1713 – 2917)	MWU	U = 132	.36	-
DMSML12	2535 (2165 – 3372)	2650 (2181 – 3580)	MWU	U = 157	.89	-
DMSMLAD	2577 (1995 – 3125)	2192 (1968 – 3078)	MWU	U = 143	.56	-
DMSMLS	2346 ± 127.90	2307 ± 159.20	t-test	t(34) = .19	.85	-454.2, 376.00
PAL						
PALFAMS	16.17 ± .62	16.83 ± .66	t-test	t(34) = .71	.74	-1.17, 2.50
PALMETS	1.00 (0.00 - 2.00)	1.00 (0.00 – 2.00)	MWU	U = 139.50	.47	-
PALTEA	4.50 (1.75 – 7.25)	3.00 (1.00 – 7.75)	MWU	U = 136	.42	-
PALTEA2	-	-	-	-	-	-
PALTEA4	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	MWU	U = 162	>.999	-
PALTEA6	0.50 (0.00 – 2.25)	0.00 (0.00 – 1.25)	MWU	U = 132	.29	-
PALTEA8	3.00 (0.75 – 5.75)	2.50 (0.00 – 5.50)	MWU	U = 148	.66	-
5-Choice						
RTIFMMT	225.40 ± 13.99	221.60 ± 11.55	t-test	t(34)= .21	.84	-40.61, 33.11
SWM						
SWMBE	3.50 (0.00 – 13.75)	9.50 (0.00 – 14.75)	MWU	U = 144.50	.58	-
SWMBE4	0.00 (0.00 – 0.50)	0.00 (0.00 – 0.00)	MWU	U = 149	.49	-
SWMBE6	0.50 (0.00 – 5.00)	1.00 (0.00 – 5.50)	MWU	U = 155	.83	-
SWMBE8	1.50 (0.00 – 7.00)	4.00 (0.00 – 13.00)	MWU	U = 134	.37	-
SWMS	6.28 ± .61	7.22 ± .51	t-test	t(34) = 1.19	.24	-.67, 2.56

Note. MWU = Mann- Whitney U test; t- test = independent t-test; YA= younger adults; MD = median; IQR = interquartile range; SEM = standard error of the mean; DMSML = DMS Mean Correct Latency; DMSML0 = DMS Mean Correct Latency (0 s delay); DMSML12 = DMS Mean Correct Latency (12 s delay); DMSML4 = DMS Mean Correct Latency (4 s delay); DMSMLAD = DMS Mean Correct Latency (All Delays); DMSMLS = DMS Mean Latency Simultaneous; PALFAMS = PAL First Attempt Memory Score; PALMETS = PAL Mean Errors to Success; PALTEA = PAL Total Errors (Adjusted); PALTEA2 = PAL Total Errors 2 Shapes (Adjusted); PALTEA4 = PAL Total Errors 4 Shapes (Adjusted); PALTEA6 = PAL Total Errors 6 Shapes (Adjusted); PALTEA8 =

PAL Total Errors 8 Shapes (Adjusted); RTIFMMT = RTI Mean Five-Choice Movement Time; SWMBE = SWM Between Errors; SWMBE4 = SWM Between Errors 4 boxes; SWMBE6 = SWM Between Errors 6 boxes; SWMBE8 = SWM Between Errors 8 boxes; SWMS = SWM Strategy (6-8 boxes).
Significant at p = .003** (Bonferroni)

Table B.21. Comparison of CANTAB performance between good and bad sleepers (sleep efficiency) in the younger adult sample

	YA good sleepers	YA bad sleepers				
	N = 18	N = 16				
CANTAB outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI
DMS						
DMSML	2413 (2186 – 2852)	2088 (1902 – 2596)	MWU	U = 98	.12	-
DMSML0	2376 (1783 – 2735)	2045 (1589 – 2433)	MWU	U = 113	.30	-
DMSML4	2336 (2093 – 3295)	2266 (1736 – 2940)	MWU	U = 124	.51	-
DMSML12	2633 (2375 – 3155)	2305 (2001 – 3208)	MWU	U = 101	.14	-
DMSMLAD	2505 (2099 – 2991)	2192 (1984 – 2744)	MWU	U = 112	.28	-
DMSMLS	2304 ± 109.4	2051 ± 147.40	t-test	t(32) = 1.64	.11	-670.30, 72.08
PAL						
PALFAMS	18.00 (16.00 – 18.00)	16.50 (15.25 – 19.75)	MWU	U = 139.50	.88	-
PALMETS	0.00 (0.00 – 1.00)	1.00 (0.00 – 2.00)	MWU	U = 110.50	.22	-
PALTEA	2.00 (2.00 – 4.00)	3.50 (.25 – 7.00)	MWU	U = 132	.69	-
PALTEA2	-	-	-	-	-	-
PALTEA4	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	MWU	U = 140	>.999	-
PALTEA6	1.00 (0.00 – 2.00)	0.00 (0.00 – 1.00)	MWU	U = 115.50	.28	-
PALTEA8	1.50 (0.00 – 2.25)	2.50 (0.00 – 4.75)	MWU	U = 110.50	.24	-
5-Choice RTI						
RTIFMMT	227.8 (206.40-248.80)	215.70 (193.10 263.30)	MWU	U = 134	.75	-

SWM						
SWMBE	4.00 (0.00 – 9.75)	13.00 (2.00 – 16.75)	MWU	U = 87.50	.048	-
SWMBE4	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	MWU	U = 124	.21	-
SWMBE6	0.00 (0.00 – .25)	2.50 (0.00 – 5.00)	MWU	U = 89.50	.04	-
SWMBE8	3.00 (0.00 – 6.00)	9.50 (.25 – 13.00)	MWU	U = 92	.07	-
SWMS	6.39 ± .63	7.13 ± .39	t-test	t(27.68) = .99	.33	-.78, 2.25

Note. MWU = Mann- Whitney U test; t- test = independent t-test; YA= younger adults; MD = median; IQR = Interquartile range; SEM = standard error of the mean; DMSML = DMS Mean Correct Latency; DMSML0 = DMS Mean Correct Latency (0 s delay); DMSML12 = DMS Mean Correct Latency (12 s delay); DMSML4 = DMS Mean Correct Latency (4 s delay); DMSMLAD = DMS Mean Correct Latency (All Delays); DMSMLS = DMS Mean Latency Simultaneous; PALFAMS = PAL First Attempt Memory Score; PALMETS = PAL Mean Errors to Success; PALTEA = PAL Total Errors (Adjusted); PALTEA2 = PAL Total Errors 2 Shapes (Adjusted); PALTEA4 = PAL Total Errors 4 Shapes (Adjusted); PALTEA6 = PAL Total Errors 6 Shapes (Adjusted); PALTEA8 = PAL Total Errors 8 Shapes (Adjusted); RTIFMMT = RTI Mean Five-Choice Movement Time; SWMBE = SWM Between Errors; SWMBE4 = SWM Between errors 4 boxes; SWMBE6 = SWM Between Errors 6 boxes; SWMBE8 = SWM Between Errors 8 boxes; SWMS = SWM Strategy (6-8 boxes).
Significant at p = .003** (Bonferroni)

Table B.22. Comparison of CANTAB performance between good and bad sleepers (TST) in the older adult sample

	OA good sleepers	OA bad sleepers				
	N = 9	N = 8				
CANTAB outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	p	95% CI
DMS						
DMSML	3528 ± 351.9	3556 ± 228.5	t-test	t(15) = .07	.95	-891.8, 948.4
DMSML0	3206 ± 302.8	3395 ± 332.4	t-test	t(14) =.42	.68	-779.6, 1157
DMSML4	3448 ± 360.9	3801 ± 325.6	t-test	t(15) =.72	.48	-693.5, 1399
DMSML12	4304 ± 600.60	4085 ± 380.60	t-test	t(15) =.30	.77	-1780, 1342
DMSMLAD	3615 ± 361.00	3791 ± 269.70	t-test	t(15) =.38	.71	-804.6, 1157
DMSMLS	3331 ± 377.80	2939 ± 146.20	t-test	t(15) = .92	.37	-1298, 513.7
PAL						
PALFAMS	11.22 ± 1.54	11.38 ± 1.70	t-test	t(15) = .07	.95	-4.72, 5.02

PALMETS	2.00 (0.50 – 3.50)	2.00 (1.25 – 2.00)	MWU	U = 34.50	.93	-
PALTEA	19.00 (8.50 – 31.50)	10.00 (8.50 – 32.25)	MWU	U = 32	.73	-
PALTEA2	0.00 (0.00 - 0.50)	0.00 (0.00 – 0.00)	MWU	U = 28	.47	-
PALTEA4	0.00 (0.00 – 2.50)	0.50 (0.00 – 3.75)	MWU	U = 32	.71	-
PALTEA6	3.00 (2.00 – 11.00)	2.50 (0.00 – 9.50)	MWU	U = 29.50	.55	-
PALTEA8	12.00 (7.50 - 23.00)	9.50 (5.25 – 23.50)	MWU	U = 27.50	.43	-
5-Choice RTI						
RTIFMMT	267.90 ± 25.53	306.10 ± 24.83	t-test	t(15) = 1.07	.30	-38.17, 114.5
SWM						
SWMBE	15.00 (8.00 – 22.00)	19.50 (4.25 – 22.00)	MWU	U = 35.50	.98	-
SWMBE4	0.00 (0.00 – 1.50)	2.00 (0.00 – 2.00)	MWU	U = 26	.37	-
SWMBE6	4.00 (0.00 – 7.00)	6.00 (0.50 – 6.75)	MWU	U = 32	.71	-
SWMBE8	13.00 (6.50 – 15.00)	11.50 (2.25 – 14.00)	MWU	U = 34	.87	-
SWMS	8.44 ± 0.60	8.88 ± 0.95	t-test	t(15) = .39	.70	-1.92, 2.78

Note. MWU = Mann- Whitney U-test; t- test = Independent t-test; OA= older adults; MD = median; IQR = interquartile range; SEM = standard error of the mean; DMSML = DMS Mean Correct Latency; DMSML0 = DMS Mean Correct Latency (0 s delay); DMSML12 = DMS Mean Correct Latency (12 s delay); DMSML4 = DMS Mean Correct Latency (4 s delay); DMSMLAD = DMS Mean Correct Latency (All Delays); DMSMLS = DMS Mean Latency Simultaneous; PALFAMS = PAL First Attempt Memory Score; PALMETS = PAL Mean Errors to Success; PALTEA = PAL Total Errors (Adjusted); PALTEA2 = PAL Total Errors 2 Shapes (Adjusted); PALTEA4 = PAL Total Errors 4 Shapes (Adjusted); PALTEA6 = PAL Total Errors 6 Shapes (Adjusted); PALTEA8 = PAL Total Errors 8 Shapes (Adjusted); RTIFMMT = RTI Mean Five-Choice Movement Time; SWMBE = SWM Between Errors; SWMBE4 = SWM Between Errors 4 boxes; SWMBE6 = SWM Between Errors 6 boxes; SWMBE8 = SWM Between Errors 8 boxes; SWMS = SWM Strategy (6-8 Boxes).
Significant at $p = .003$** (Bonferroni)

Table B.23. Comparison of CANTAB performance between good and bad sleepers (sleep efficiency) in the older adult sample

	OA good sleepers	OA bad sleepers				
	N = 8	N = 8				
CANTAB outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI

DMS						
DMSML	3047 ± 273.90	3472 ± 189.80	t-test	t(14) = 1.28	.22	-289.4, 1140
DMSML0	3052 ± 285.60	3019 ± 319.10	t-test	t(13) = .08	.94	-955.2, 889.3
DMSML4	3072 ± 284.10	3929 ± 352.50	t-test	t(14) = 1.89	.08	-113.8, 1828
DMSML12	3111 (2527 – 3988)	3840 (3268 – 4428)	MWU	U = 16	.10	-
DMSMLAD	3136 ± 276.10	3696 ± 232.80	t-test	t(14) = 1.55	.14	-214.3, 1335
DMSMLS	2855 ± 349.10	3000 ± 260.80	t-test	t(14) = .33	.74	-789.4, 1080
PAL						
PALFAMS	12.75 ± 1.32	10.63 ± 2.18	t-test	t(14) = .83	.42	-7.59, 3.34
PALMETS	1.63 ± .46	1.25 ± .25	t-test	t(14) = .72	.49	-1.50, 0.75
PALTEA	16.75 ± 4.47	26.13 ± 8.06	t-test	t(14) = 1.02	.33	-10.40, 29.15
PALTEA2	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	MWU	U = 28	>.999	-
PALTEA4	0.00 (0.00 – 1.50)	2.50 (0.00 – 4.00)	MWU	U = 19.50	.18	-
PALTEA6	2.00 (0.50 – 9.75)	4.00 (0.75 – 15.00)	MWU	U = 22.50	.34	-
PALTEA8	9.50 (6.25 – 13.75)	16.50 (3.50 – 28.00)	MWU	U = 31.50	.98	-
5-Choice RTI						
RTIFMMT	264.2 ± 19.49	269.2 ± 28.86	t-test	t(14) = .15	.89	-69.63, 79.75
SWM						
SWMBE	14.38 ± 2.82	19.38 ± 1.71	t-test	t(14) = 1.52	.15	-2.07, 12.07
SWMBE4	1.50 (0.00 – 2.00)	1.00 (0.00 – 2.00)	MWU	U = 30	.97	-
SWMBE6	3.50 ± 1.09	5.00 ± .93	t-test	t(14) = 1.05	.31	-1.56, 4.56
SWMBE8	9.63 ± 1.97	13.25 ± 1.15	t-test	t(14) = 1.59	.13	-1.27, 8.52
SWMS	8.25 ± .96	9.75 ± .45	t-test	t(14) = 1.41	.18	-0.77, 3.78

Note. MWU = Mann- Whitney U test; t- test = independent t-test; YA= younger adults; MD = median; IQR = interquartile range; SEM = standard error of the mean; DMSML = DMS Mean Correct Latency; DMSML0 = DMS Mean Correct Latency (0 s delay); DMSML12 = DMS Mean Correct Latency (12 s delay); DMSML4 = DMS Mean Correct Latency (4 s delay); DMSMLAD = DMS Mean Correct Latency (All Delays); DMSMLS = DMS Mean Latency Simultaneous; PALFAMS = PAL First Attempt Memory Score; PALMETS = PAL Mean Errors to Success; PALTEA = PAL Total Errors (Adjusted); PALTEA2 = PAL Total Errors 2 Shapes (Adjusted); PALTEA4 = PAL Total Errors 4 Shapes (Adjusted); PALTEA6 = PAL Total Errors 6 Shapes (Adjusted); PALTEA8 = PAL Total Errors 8 Shapes (Adjusted); RTIFMMT = RTI Mean Five-Choice Movement Time; SWMBE = SWM Between Errors; SWMBE4 = SWM Between Errors 4 boxes; SWMBE6 = SWM Between Errors 6 boxes; SWMBE8 = SWM Between Errors 8 boxes; SWMS = SWM Strategy (6-8 boxes).
Significant at p = .003** (Bonferroni)

Table B.24. Sample characteristics for the sleep deprivation study

	Rested		Deprived	
	Total	%	Total	%
Age				
18	5	18.52 %	1	7.69 %
19	6	22.22 %	0	0 %
20	8	29.63 %	1	7.69 %
21	2	7.41 %	2	15.39 %
22	3	11.11 %	3	23.08 %
23	1	3.70 %	1	7.69 %
24	0	0 %	0	0 %
25	2	7.41 %	0	0 %
26	0	0 %	2	15.39 %
27	0	0 %	0	0 %
28	0	0 %	0	0 %
29	0	0 %	1	7.69 %
30	0	0 %	0	0 %
31	0	0 %	0	0 %
32	0	0 %	0	0 %

33	0	0 %	1	7.69 %
34	0	0 %	1	7.69 %
Sex				
Female	14	51.85 %	6	46.15 %
Male	13	48.15 %	7	53.85 %
Ethnicity				
First nations	1	3.70 %	0	0 %
Black	0	0 %	0	0 %
Hispanic	0	0 %	2	15.39 %
Fijian	1	3.70 %	0	0 %
Indian	3	11.11 %	1	7.69 %
Asian	11	40.74 %	4	14.81 %
Indo-Mauritian	1	3.70 %	0	0 %
Sri-Lankan	0	0 %	1	7.69 %
Middle-eastern	2	7.41 %	2	15.39 %
Middle eastern - white	1	3.70 %	0	0 %
White	7	25.93 %	3	23.08 %

Table B.25. Comparison of PVT performance between the rested and sleep deprived participants

	Rested	Deprived				
	N = 27	N = 13				
MST outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI
PVT lapse	1.00 (0.00 – 1.00)	1.00 (0.00 – 2.00)	MWU	U = 145	.37	-
10% fastest RT	262.00 (243.20 – 278.70)	262.30 (245.00 – 269.10)	MWU	U = 169	.86	-
10% slowest RT	434.80 (404.80 – 475.00)	488.80 (424.30 – 535.10)	MWU	U = 125	.15	-
1/Mean RT	3.18 ± .06	3.10 ± .07	t-test	t(38) = .89	.38	-.28 - .11
Cognitive slowing	2.26 ± .07	2.10 ± .10	t-test	t(38) =1.29	.21	-.41 - .09

Note. MWU = Mann- Whitney U test; t- test = independent t-test; MD = median; IQR = interquartile range; SEM = standard error of the mean.
Significant at $p = .01$* (Bonferroni)

Table B.26. Comparison of MST performance between the rested and sleep deprived participants

	Rested	Deprived				
	N = 23	N = 9				
MST outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI
LDI	.33 (.29 - .55)	.37 (.27 - .40)	MWU	U = 98	.83	-
REC	.86 (.79 - .89)	.89 (.81 - .94)	MWU	U = 71	.18	-
L1	.22 ± .04	.16 ± .04	t-test	t(30) = 1.00	.32	-.21, .07
L2	.38 ± .04	.20 ± .04	t-test	t(30) = 2.28	.03	-.33, -.02
L3	.36 (.29 - .54)	.39 (.29 - .49)	MWU	U = 101	.93	-
L4	.49 ± .05	.41 ± .06	t-test	t(30) = .89	.38	-.26, .10
L5	.50 ± .04	.53 ± .05	t-test	t(30) = .38	.71	-.13, .19

Note. MD = median; IQR = interquartile range; SEM = standard error of the mean; LDI = Lure Discrimination Index; REC= Recognition memory; L1 = Lure bin 1; L2 = Lure bin 2; L3 = Lure bin 3; L4 = Lure bin 4; L5 = Lure bin 5.
Significant at $p = .007$* (Bonferroni)

Table B.27. Comparison of CANTAB performance between the rested and sleep deprived participants

	Rested	Deprived				
	N = 27	N = 13				
CANTAB outcomes	Mean ± SEM MD (IQR)	Mean ± SEM MD (IQR)	Test	Test statistic	*p*	95% CI
DMS						
DMSML	2835 ± 148.80	2983 ± 237.20	t-test	t(38) = .55	.59	-398.8, 694.6
DMSML0	2259 (2011 – 3032)	2986 (1894 – 3248)	MWU	U = 158	.63	-
DMSML4	2942 ± 183.40	2951 ± 155.10	t-test	t(38) = .03	.98	-570.8, 588.9
DMSML12	3044 (2553 – 3751)	3665 (2982 – 4187)	MWU	U = 133	.23	-
DMSMLAD	2924 ± 164.60	3188 ± 266.60	t-test	t(38) = .88	.39	-344.3, 872.2
DMSMLS	2598 ± 140.40	2407 ± 182.50	t-test	t(38) = .80	.43	-674.1, 293.1
PAL						
PALFAMS	15.56 ± .53	17.23 ± .61	t-test	t(38) = 1.91	.06	-.10, 3.45
PALMETS	1.00 (0.00 – 2.00)	1.00 (0.00 – 1.50)	MWU	U = 128	.15	-
PALTEA	6.00 (2.00 – 8.00)	4.00 (1.00 – 5.00)	MWU	U= 101	.03	-
PALTEA2	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	MWU	U = 169	>.999	-
PALTEA4	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	MWU	U = 156	.54	-
PALTEA6	0.00 (0.00 – 3.00)	0.00 (0.00 – 1.00)	MWU	U = 141	.25	-
PALTEA8	4.00 (2.00 – 7.00)	2.00 (1.00 – 4.00)	MWU	U = 117.5	.09	-
5-Choice RTI						
RTIFMMT	242.90 ± 9.30	235.70 ± 14.65	t-test	t(38) = .43	.67	-41.27, 26.77
SWM						
SWMBE	12.00 (2.00 – 18.00)	1.00 (0.00 – 11.00)	MWU	U = 97	.02	-

SWMBE4	0.00 (0.00 – 1.00)	0.00 (0.00 – 2.00)	MWU	U = 171.5	.86	-
SWMBE6	2.00 (0.00 – 6.00)	0.00 (0.00 – 3.00)	MWU	U = 116	.07	-
SWMBE8	7.00 (0.00 – 12.00)	0.00 (0.00 – 7.00)	MWU	U = 110	.052	-
SWMS	7.37 ± .49	5.69 ± .79	t-test	t(38) = 1.88	.07	-3.49, .13

Note. MWU = Mann- Whitney U test; t- test = independent t-test; MD = median; IQR = interquartile range; SEM = standard error of the mean; DMSML = DMS Mean Correct Latency; DMSML0 = DMS Mean Correct Latency (0 s delay); DMSML12 = DMS Mean Correct Latency (12 s delay); DMSML4 = DMS Mean Correct Latency (4 s delay); DMSMLAD = DMS Mean Correct Latency (All Delays); DMSMLS = DMS Mean Latency Simultaneous; PALFAMS = PAL First Attempt Memory Score; PALMETS = PAL Mean Errors to Success; PALTEA = PAL Total Errors (Adjusted); PALTEA2 = PAL Total Errors 2 Shapes (Adjusted); PALTEA4 = PAL Total Errors 4 Shapes (Adjusted); PALTEA6 = PAL Total Errors 6 Shapes (Adjusted); PALTEA8 = PAL Total Errors 8 Shapes (Adjusted); RTIFMMT = RTI Mean Five-Choice Movement Time; SWMBE = SWM Between Errors; SWMBE4 = SWM Between Errors 4 boxes; SWMBE6 = SWM Between Errors 6 boxes; SWMBE8 = SWM Between Errors 8 boxes; SWMS = SWM Strategy (6-8 boxes).
Significant at p = .003** (Bonferroni)

Appendix C.

Figures

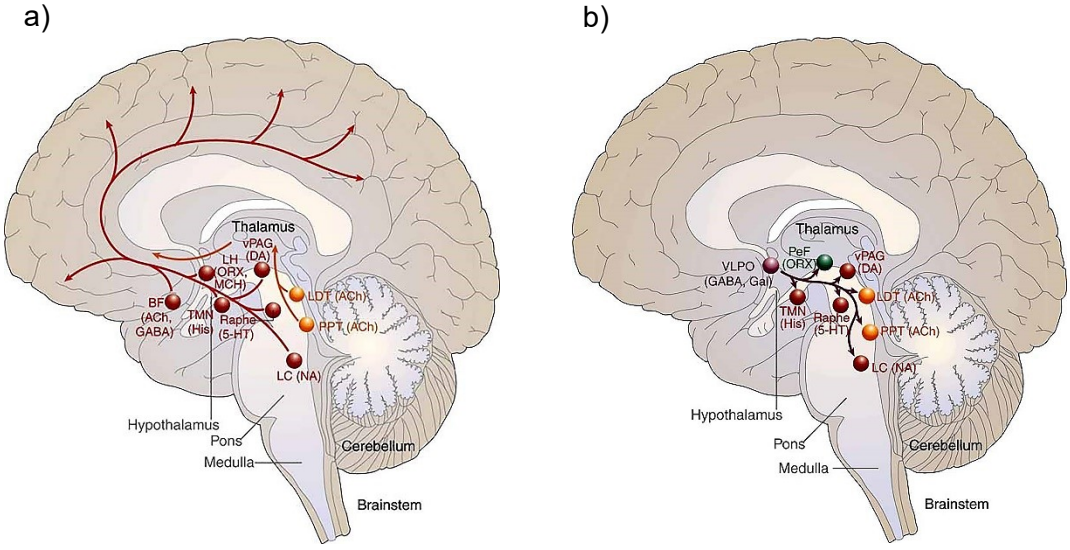

Figure C.1. a) Brain regions involved in wakefulness and b) Brain regions involved in NREM and REM sleep.

Note: Adapted from Saper et al., 2005.

Appendix D.

Questionnaires

Sleep diary

Please complete in the morning and describe the last 24 hours
Please describe your main sleep in bed in Q1-8 and any other sleep as Naps (Q10)
If you have not slept in the past 24 hours, answer Q1-6 and Q10 as '0'

Today's Date (mm/dd/yy):

Lights out: hr min am / pm **Lights on: hr min am / pm**

<u>Main Questions</u>

1. **What time did you try to fall asleep? hr min am / pm**
2. **How long did it take you to fall asleep? hr min am / pm**
3. **What time did you finally wake up? hr min am / pm**
4. **How long did you sleep? hr min am / pm**
5. **How long did you stay in bed before getting up? hr min am / pm**
6. **How many times did you awaken? List each: when and for how long?**
    a. **When? hr min am / pm For how long? hr min**
    b. **When? hr min am / pm For how long? hr min**
    c. **When? hr min am / pm For how long? hr min**
    d. **When? hr min am / pm For how long? hr min**
    e. **When? hr min am / pm For how long? hr min**
7. **Did anything disturb your sleep? Circle all if anything.**
    a. **Noise / Work Duties / Physical Discomfort / Other: .**

8. **How did you sleep last night? (mark with an X on the line)**
   Poorly----------
   Great

9. **How do you feel right now? (mark with an X on the line)**
   Sleepy----------
Alert

10. **Did you nap yesterday? If so, list each: when the nap started and when it ended.**
    a. **Nap start ____hr ____min am / pm Nap end ____hr ____min am / pm**
    b. **Nap start ____hr ____min am / pm Nap end ____hr ____min am / pm**
    c. **Nap start ____hr ____min am / pm Nap end ____hr ____min am / pm**
11. **Did you take any medications yesterday? [Yes / No / Decline] If yes, list all below.**
12. **Did you exercise yesterday? [Yes / No / Decline] If yes, please describe below.**

<u>Women Only</u>

1. **Did you have any menstrual bleeding yesterday? [Yes/No]**
2. **Date of last period prior to starting this log (mm/dd/yy):**