THE RELATIONSHIP BETWEEN SLEEP DISTURBANCES AND EPISODIC MEMORY IN OLDER ADULTS

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DEDICATION

To my parents and family

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Table of Contents

List of Tables

List of Figures

Abstract

Impaired episodic memory in older adults has been posited to be related to sleep disturbances which are revealed by self-reported questionnaires and objective devices but the relationship between these two measured results is unclear. Sleep disturbances have been tied to declines in attention, executive function, and cognitive reserve, which may contribute to impaired episodic memory. However, how sleep disturbances relate to these cognitive functions and in turn influence episodic memory remains unclear. Age and depressive symptoms are correlated with sleep disturbances and episodic memory decline in older adults; however, the role of age and depressive symptoms in explaining the relationship between sleep disturbances and episodic memory remains unclear

The specific aims were (a) to determine the conceptual structure of sleep disturbances in older adults; and (b) to determine the relationship between sleep disturbances and episodic memory in older adults, including the roles of attention, executive function, cognitive reserve, depressive symptoms, and aging in the relationship.

This descriptive study included a convenience sample of (N=62) older adults (age 60-88). Two sleep questionnaires and actigraphy were used to measure sleep; the Hopkins Verbal Learning Test-Revised was used to assess episodic memory; the CogState computerized battery was used to evaluate attention and executive function; and the Wide Range Achievement Test 4-Reading subtest was used to measure cognitive reserve. Descriptive statistics, Pearson's correlation, exploratory factor analysis, and hierarchical multiple regression analyses were conducted to analyze data.

Self-reported sleep disturbances significantly correlated with objective sleep time and wakefulness during sleep periods, but this relationship was only substantial for objective sleep time. In older adults, more objective difficulty in falling and staying asleep, better executive function, more cognitive reserve and unexpectedly, higher level of daytime sleepiness explained better episodic memory after controlling for the covariates. The influence of sleep disturbances on episodic memory was stronger among those participants with more, as compared to less depressive symptoms. The study results suggest some possible directions to develop sleep interventions to prevent episodic memory declines in older adults. Future studies may focus on improving daytime sleepiness and difficulty in falling and staying asleep to prevent episodic memory declines.

Chapter One

Introduction

This chapter is organized into five sections. In the first section, the knowledge background of this dissertation research is introduced. In the second section, the problem statement, knowledge gaps and conceptual framework are presented. In the third section, the structure of this dissertation paper is introduced to guide readers. In the fourth section, the definitions of variables (i.e., episodic memory, sleep, depressive symptoms, attention, executive function, and cognitive reserve) are introduced and theoretical background to support the relationship between sleep and memory and the role of the other factors (age, depressive symptoms, attention, executive function, and cognitive reserve) are presented. In the final section, the summary of this chapter is presented.

Episodic memory is a subtype of declarative or explicit memory, involving learning, storing, and retrieving information about personal experience from daily life (Dickerson & Eichenbaum, 2010). Episodic memory can be stored for as little as minutes to years (Budson & Price, 2005). These memories contain a variety of information including the time, location, and facts of an event (Dickerson & Eichenbaum, 2010). The formation of such memories (i.e., acquisition, consolidation, and retrieval) (Abel & Lattal, 2001; Marshall & Born, 2007) requires support from several regions of the brain including the hippocampus (the most important area), the parahippocampus, the prefrontal cortex, the associated neocortical areas, the medial occipital cortex, the inferotemporal cortex, the retrosplenial/posterior cingulate, and the temporal-parietal

junction (Brand & Markowitsch, 2008; Budson & Price, 2005; Dickerson & Eichenbaum, 2010; Moscovitch, Winocur, Ryan, & Nadel, 2008).

Episodic memory is critical not only for the storage of personal experience but also learning behavior. Episodic memory is involved in various types of learning processes about personal experiences, personal meaning (Dickerson & Eichenbaum, 2010), early semantic learning (Merritt, Hirshman, Zamani, Hsu, & Berrigan, 2006), and skill learning (Beaunieux, Hubert, Pitel, Desgranges, & Eustache, 2009). Importantly, episodic memory is associated with functional ability [i.e., activities of daily living (ADLs) and instrumental activities of daily living (IADLs)] in older adults with and without cognitive impairment. If older adults experience a decline in episodic memory, this is often the best predictor of the extent of decrease in functional ability in this population (Burton, Strauss, Hultsch, & Hunter, 2006; Goldberg et al., 2010; Tomaszewski Farias et al., 2009). Because functional ability is important for humans' independence, the decline in functional ability limits the ability to live independently (Burton et al., 2006) and is significantly associated with longer hospital stays and an increase in the number of nursing home placements (Fogel, Hyman, Rock, & Wolf-Klein, 2000). In fact, older adults with poor functional ability are more likely to be discharged to nursing homes than those with better functional ability discharged home (Fogel et al., 2000).

Impaired memory function, including impaired episodic memory, has been associated with increased mortality. According to a study by Pressler, Kim, Riley, Ronis, and Gradus-Pizlo (2010), memory dysfunction is associated with an increase in mortality of patients with heart failure and low ejection fraction. Declines in memory function predicted increased mortality in older adults, with dementia (Lee et al., 2006) and without dementia (Lavery, Dodge, Snitz, &

Ganguli, 2009). Thus, it is important to investigate the factors that contribute to the decline in episodic memory performance.

Decline in episodic memory is associated with a variety of factors, one of the most important of which is sleep disturbances. Sleep disturbances are common for many older adults. According to a community-based, observational study by the National Institute of Aging (n> 9000), more than 50% of older adults with a mean age of 74.1 across the United States complained of chronic sleep disturbances (Foley et al., 1995). Among adults with a mean age of 85.3 years living in assisted living facilities (n=121), 65% subjectively reported poor sleep quality (Martin, Fiorentino, Jouldjian, Josephson, & Alessi, 2010). The characteristics of self-reported and objectively measured age-related sleep disturbances in older adults are presented in Table 1.1. (Edwards et al., 2010; Ensrud et al., 2009; Espiritu, 2008).

Sleep disturbances have been posited to be associated with declines in episodic memory because sleep plays an important role in the encoding and consolidation of episodic memory. Several studies have indicated that self-reported sleep disturbances were negatively correlated with performance of episodic memory in older adults: shorter ($\leq$ 5 hours) or longer ($\geq$ 9 hours) sleep time (Ferrie et al., 2011; Kronholm et al., 2009; Loerbroks, Debling, Amelang, & Sturmer, 2010; Schmutte et al., 2007; Tworoger, Lee, Schernhammer, & Grodstein, 2006; Xu et al., 2011), a decrease in sleep efficiency (Westerberg et al., 2010), daytime tiredness and fatigue (Kronholm et al., 2009; Xu et al., 2011), difficulty in falling and staying asleep (Tworoger et al., 2006; Westerberg et al., 2010), increased sleep onset latency (Schmutte et al., 2007), poor sleep quality (Nebes et al., 2009; Sutter, Zollig, Allemand, & Martin, 2012), daytime sleepiness (Bonanni et al., 2005; Ohayon & Vecchierini, 2002), and increased daytime napping (Ohayon & Vecchierini,

2002; Xu et al., 2011). Self-reported sleep time has a reversed U-shape association with episodic memory performance. Older adults with 6 to 8 hours of sleep time had better performance in

Table 1.1

The Characteristics of Sleep Disturbances of Older Adults

	Sleep characteristics
Self-reported	Difficulty in falling asleep or maintaining sleep
	Increased long fragmented sleep (wakefulness after sleep onset> five minutes)
	More daytime sleepiness
	Early morning awakening
	Decreased total sleep duration (total hours of sleep while in bed)
	Decreased sleep efficiency (percentage of total sleep duration while in the bed)
	Increased sleep latency (amount of time until sleep onset while in bed)
	Increased number and length of daytime napping
	Poor sleep quality
Objectively measured	Reduction of total sleep duration (around 10 minute per decade)
	Decreased sleep efficiency
	Decreased REM sleep (from the age of 60)
	Decreased number of sleep cycles per night
	Increased sleep latency
	Increased stage one and two of NREM sleep
	Increased number of long fragmented sleep episodes (waking up after sleep onset while in bed > five minutes

Note. NREM= non-rapid eye movement; SWS= slow wave sleep; REM=rapid eye movement.

episodic memory. On the other hand, the adults with ≤ 5 hours and ≥ 9 hours had poor performance on episodic memory tests (Ferrie et al., 2011; Kronholm et al., 2009; Loerbroks et al., 2010; Schmutte et al., 2007; Tworoger et al., 2006; Xu et al., 2011).

In addition to self-reported sleep disturbances, objectively measured sleep parameters including total sleep time (Cochrane, Robertson, & Coogan, 2012; Gamaldo, Allaire, & Whitfield, 2008; Hart, Morin, & Best, 1995; Westerberg et al., 2010), the time and percentage of slow wave sleep (SWS) which is the stage 3 and 4 of non-rapid eye movement(NREM) sleep (Backhaus et al., 2007), sleep fragmentation, sleep latency (Westerberg et al., 2010) , average NREM/rapid eye movement (REM) cycle, proportion of total time spent in NREM/REM cycles over total sleep time (Mazzoni et al., 1999), and fragmented sleep-wake rhythm (Oosterman, van Someren, Vogels, Van Harten, & Scherder, 2009) have been shown to be significantly correlated with episodic memory performance among older adults.

Studies have indicated that sleep may improve episodic memory. After one night of normal sleep, older adults performed better on episodic memory tests (Aly & Moscovitch, 2010; Fenn, Gallo, Margoliash, Roediger, & Nusbaum, 2009; Hornung, Regen, Danker-Hopfe, Schredl, & Heuser, 2007; Spencer, Gouw, & Ivry, 2007; Westerberg et al., 2012; Wilson, Baran, Pace-Schott, Ivry, & Spencer, 2012). Alternatively, the artificial restriction or deprivation of sleep (e.g. total sleep time, REM sleep deprivation, stage 2 NREM sleep deprivation, SWS disruption) was associated with a decline in episodic memory performance (Backhaus et al., 2007; Stenuit & Kerkhofs, 2008; Van Der Werf, Altena, Vis, Koene, & Van Someren, 2011). However, despite all of the reported associations, it is still unclear which measures of self-reported and objective sleep disturbances are most strongly associated with episodic memory performance and might even be able to predict changes in episodic memory.

In addition to their impact on episodic memory, sleep disturbances influence attention, executive function, and cognitive reserve which in turn, together, can affect episodic memory. Older adults with self-reported daytime sleepiness, shorter sleep time, and taking sleep medicine had more impaired attention than a group without these sleep disturbances (Ohayon & Vecchierini, 2002) and this impaired attention has been posited to contribute to episodic memory deficits (Cole & Richard, 2005). Additionally, total sleep deprivation (Harrison & Horne, 1999; Harrison, Horne, & Rothwell, 2000) and fragmentation of sleep-wake rhythm (Oosterman et al., 2009) have been associated with poor executive function, which may affect the formation of episodic memory, particularly in encoding and retrieval, the first and third stage of memory formation (Brand & Markowitsch, 2008). Executive function can significantly influence the hippocampus volume, which is the most important brain region for episodic memory, and white matter hyper-intensities across the whole brain, and in turn affect episodic memory performance (Parks et al., 2011).

Although the associations of attention and executive function with sleep are reasonably well understood, the association between cognitive reserve and sleep is still an open question. Neuroprotective functions of cognitive reserve may be playing a role in the mediation of damage to cognitive function (e.g., executive function) from sleep disturbances (Zimmerman, Bigal, Katz, Brickman, & Lipton, 2012). However, sleep disturbances may be reducing the neuroprotective effects of cognitive reserve by increasing negative neuroplasticity (e.g., decrease in dendritic connection or decline of brain size) (Vance, Roberson, McGuinness, & Fazeli, 2010).

In addition to attention, executive function, and cognitive reserve, ageing and depressive symptoms have been posited to be related to sleep disturbances and in turn influence episodic memory. With aging process, around 50% of older adults who are over 65 years old complain

sleep disturbances (Foley et al., 1995) and the mechanism of sleep disturbances in older adults is associated with the degeneration of the suprachiasmatic nucleus (SCN) system in the hypothalamus which is the modulator of sleep-wake cycle (Hofman & Swaab, 2006; Wu & Swaab, 2007). Aging is associated with cognitive decline, particularly in learning and memory. This memory deficit may be related to the changes in the neural function in the hippocampus that occur with aging (Rosenzweig & Barnes, 2003). The age-related deficit in episodic memory can be attributed to a failure to differentiate re-experienced memory and newly encoded information, particularly spatial information, and to a dysfunction of episodic memory retrieval (Dickerson & Eichenbaum, 2010).

In addition to aging, depressive symptoms have been associated with sleep disturbances and may influence episodic memory in older adults. Older adults with greater depressive symptoms had more sleep disturbances (i.e. reduced sleep efficiency, increased sleep latency, longer fragmented sleep episodes, more number of fragmented sleep episodes, poor sleep quality, and increased daytime sleepiness) (Maglione et al., 2012; Paudel et al., 2008). Sleep disturbances (i.e. difficulty in falling asleep and sleepiness) increased the risk of depression after one year among the individuals older than 50 (Roberts, Shema, Kaplan, & Strawbridge, 2000). On the other hand, the individuals with poor sleep quality had more depressive symptoms (Nebes, Buysse, Halligan, Houck, & Monk, 2009). Depression is considered a significant cause of chronic insomnia and insomnia is a frequent symptom of depression (Franzen & Buysse, 2008). In summary, sleep disturbances and depressive symptoms are correlated with each other. Moreover, depression may contribute to atrophy of the hippocampus, the most important brain region for episodic memory (Fotuhi, Do, & Jack, 2012) and is significantly correlated with

decline in episodic memory in older adults (Beaudreau & O'Hara, 2009; Gonzalez, Bowen, & Fisher, 2008; Panza et al., 2009).

Problem Statement

There are seven knowledge gaps that can be drawn by the above-mentioned literature review. First, although it is known that some self-reported sleep problems are associated with decline in episodic memory (Bonanni et al., 2005; Ferrie et al., 2011; Haimov, 2006; Kronholm et al., 2009; Loerbroks et al., 2010; Ohayon & Vecchierini, 2002; Schmutte et al., 2007; Sutter et al., 2012; Tworoger et al., 2006; Westerberg et al., 2010; Xu et al., 2011), the relative contribution of each and the mechanisms involved in these factors affecting episodic memory remain unclear.

Second, in addition to self-reported sleep problems, some objectively measured sleep disturbances (i.e., decreased total sleep time, reduced sleep efficiency, increased sleep latency, more number and length of long fragmented sleep episodes) may affect episodic memory performance among older adults, though their relative contributions remains poorly characterized. For instance, Hart et al. (1995) (n=78) indicated that total sleep time, as measured by a polysomnography was related to episodic memory in healthy older adults (R^2=0.13, p<.01) (Hart et al., 1995). However, this study did not mention whether objective total sleep time correlated positively or negatively with the performance on episodic memory. Another study by Westerberg et al. (2010) (n=20) indicated that total sleep time, sleep latency and sleep fragmentation, measured by a wrist actigraph device for 14 continuous days were negatively associated with performance of episodic memory in healthy older adults and patients with amnestic mild cognitive impairment (aMCI) (Westerberg et al., 2010). However, the sample size of this study was small, only 20 participants which was too small to generalize the results. This small sample

made it difficult to determine the influence of sleep disturbances on episodic memory only among healthy older adults. It appears clear, then, based on the above studies, the association among objectively measured total sleep disturbances and episodic memory in older adults still needs more investigation.

Third, the association between self-reported and objectively measured sleep disturbances remains unclear. Hart et al. (1995) reported that sleep efficiency and fragmented sleep as recorded in a sleep diary and from a polysomnography were significantly correlated ($r=0.23$, $p<.05$ and $r=0.33$, $p<.01$, respectively) in older adults. However, few studies were found that have yet explored the association between other subjective and objective sleep disturbances.

Fourth, according to the literature review, attention and executive function, which have been affected by sleep disturbances, may be correlated with performance on episodic memory in older adults. However, few studies have investigated the possible moderating or mediating effects of attention and executive function on the relationship between sleep disturbances and episodic memory.

Fifth, although it has been inferred that poor sleep may contribute to decline of cognitive reserve (Vance et al., 2010), no studies were found during this literature review that clearly indicated the effect of sleep on cognitive reserve and the effects of cognitive reserve in combination with sleep disturbances on episodic memory.

Sixth, although depressive symptoms have been posited to be significantly associated with declines in episodic memory (Beaudreau & O'Hara, 2009; Gonzalez et al., 2008; Panza et al., 2009) and sleep disturbances (Maglione et al., 2012; Paudel et al., 2008) among older adults, there is a lack of studies investigating the possible moderating effect of depressive symptoms on the relationship between sleep disturbances and episodic memory in older adults.

Seventh, it is clear that age-related degeneration is significantly related to sleep disturbances and a deficit of episodic memory. However, the possible moderating effect of aging in the relationship of sleep disturbances and episodic memory performance still needs more investigation.

Thus, more studies are needed to evaluate the relationship between sleep disturbances and episodic memory and investigate the possible effect of attention, executive function, cognitive research function, aging, and depressive symptoms in this relationship after accounting for the possible covariates such as gender, education, health conditions, and body mass index (BMI). The conceptual framework developed from the literatures to describe the relationships among sleep disturbances, episodic memory, aging, depressive symptoms, attention, executive function, and cognitive reserve is presented in Figure 1.1.

Implications for the Metaparadigm of Nursing and Nursing Science

The purpose of this study is consistent with the concepts of the metaparadigm of nursing and is closely tied to the foci of nursing science. The concepts of the metaparadigm of nursing include person, health, nursing, and environments (Thorne et al., 1998) which are related to the major variables of this study. One of the major variables, sleep, is a basic physiological function of a person (Guilleminault & Kreutzer, 2003) and can influence human health, both physiological and mental. Sleep is related to environment. Some environmental factors such as noise can induce poor sleep (Edwards et al., 2010) and improvement of environment may reduce sleep problems. The sleep interventions such as sleep hygiene can be administered and evaluated by nurses. In addition to sleep, another major variable, episodic memory, is a fundamental cognitive function of a person. Poor episodic memory can contribute to impaired ability to maintain human health (Burton et al, 2006; Goldberg et al., 2010; Tomaszewski Farias et al.,

2009) and to learn new knowledge and skills (Dickerson & Eichenbaum, 2010), which may influence the efficiency of health education offered by nurses in clinical settings.

Nursing science is focusing in the holistic health of humans (Fuller, 1978), the perceived phenomena (e.g., pain or fatigue) that affect human health (National Institute of Nursing Research, 2011; Algase & Whall, 1993), mortality, quality of life, self-management, and health promotion (National Institute of Nursing Research, 2011). Both sleep and episodic memory are fundamental for a person's quality of life (Maki et al., 2014; Manocchia, Keller, & Ware, 2001) and are associated with mortality (Lavery et al., 2009; Lee et al., 2006; Pressler et al., 2010; Xiao, Keadle, Hollenbeck, & Matthews, 2014), thus, they clearly both fall within the foci of nursing science and are sensitive to nursing intervention (National Institute of Nursing Research, 2011). In this study, the relationship between sleep and episodic memory is more understood and the possible roles of related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve) were examined. These results can increase the understanding of the knowledge base about the association between sleep, episodic memory, and related factors which closely tie to the interests of nursing science. Moreover, a clear understanding of the relationship between sleep disturbances and episodic memory would be needed before sleep interventions can be developed for nursing aimed at improving episodic memory. For instance, a clearer understanding is needed as to which sleep characteristics are more strongly correlated with episodic memory and which related factors (e.g., aging or depressive symptoms) may influence the relationship. That may offer a direction for designing sleep interventions for nurses to improve episodic memory and the problems (i.e., decline in functional status and higher mortality) following impaired episodic memory.

Structure of the Dissertation

This dissertation follows a three-manuscript format consisting of five chapters: an introduction; three manuscript-type papers; and summary. In the first chapter, background knowledge, the problem statement, and the theoretical perspective are presented. Chapter 2, which is the first paper, is a systematical review of current publications that investigated the relationship between sleep disturbances and episodic memory. Current knowledge gaps are identified. Chapter 3, the second paper, was completed to investigate the relationship between the self-reported sleep problems and objectively measured sleep characteristics. Chapter 4, the third paper, was conducted to explore whether sleep disturbances including self-reported and objectively measured and related factors (i.e., ageing, depressive symptoms, attention, executive function, and cognitive reserve) can predict episodic memory performance in older adults after controlling covariates such as gender, educational yeas, chronic conditions, and body mass index. In this chapter, the role of age, depressive symptoms, attention, executive function, and cognitive reserve in the relationship between sleep disturbances and episodic memory were explored. Chapter 5, the final chapter, provides a summary of the results, overall conclusion, limitations, and clinical implications of these three papers, and directions for future studies.

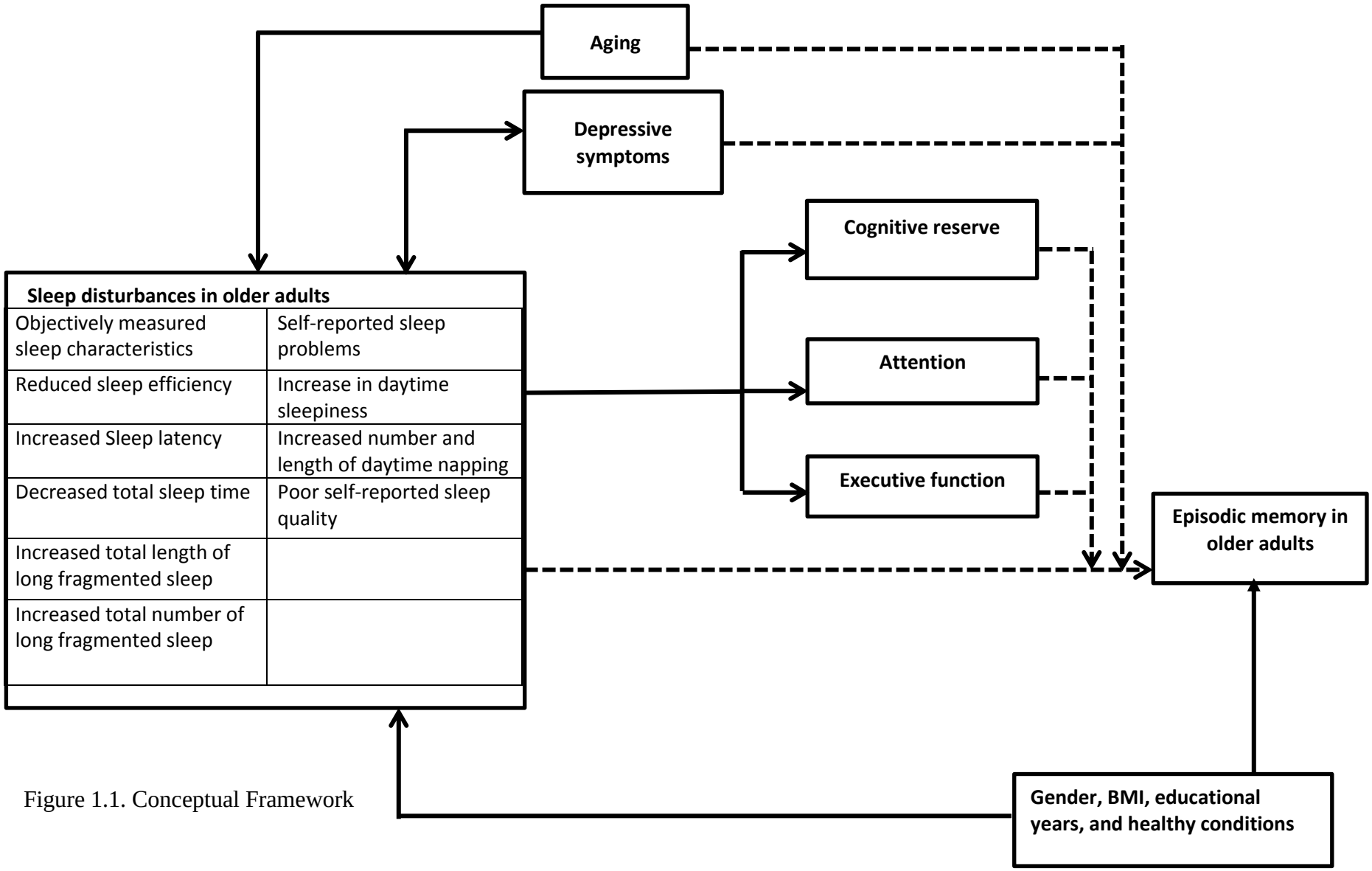

Figure 1.1. Conceptual Framework

Theoretical Perspectives

In this section, the theoretical perspectives of episodic memory, sleep, the relationship between sleep and episodic memory and the roles of the other related factors (i.e., attention, executive function, and cognitive reserve) are discussed.

Episodic Memory

The conceptual definition of episodic memory.

Episodic memory is a subdivision of the long-term declarative memory and conceptually defined as the process of acquiring, consolidating, and retrieving information about personal experience from daily life. Episodic memory consists of various components of information from experienced events including spatial (where), temporal (when), and factual (what) information (Dickerson & Eichenbaum, 2010; Squire & Kandel, 2009).

The neural basis of episodic memory.

Episodic memory is supported by a neural network consisting of widespread associated neocortical areas and the medial temporal lobes including both the hippocampus and the parahippocampus belonging to the limbic system (Dickerson & Eichenbaum, 2010). The hippocampus, involved in episodic memory formation, consists of several subdivisions: the dentate gyrus, the CA3 field, the CA1field, and the subiculum. These subdivisions of the hippocampus are connected by an internal and unidirectional connection, which starts at the dentate gyrus, continues through the CA3 field, then the CA1 field, and ends in the subiculum. Apart from the hippocampus, the associated neocortical areas and the parahippocampus are involved in formation of episodic memory and connect to the hippocampus. There are inputted projections from the associate neocortical areas which converge in the parahippocampus and then be sent to each subdivision of the hippocampus. On the other hand, the feedback output of

the hippocampus arises in the CA1 field and the subiculum projects to the associated neocortical areas through the parahippocampus (Dickerson & Eichenbaum, 2010). The parahippocampus consists of the perirhinal cortex, the postrhinal (parahippocampal) cortex, and the entorhinal cortex. The associated neocortical areas include the prefrontal cortex and the some areas of the parietal and temporal cortex. This neural network constructs the neurocircuitry to support the function of episodic memory (Dickerson & Eichenbaum, 2010).

The age-related deficits of episodic memory.

As adults age, the function of the hippocampus typically declines. This decline starts as early as 31 years. Due to this hippocampal dysfunction, older adults encode new information more slowly with an average delayed onset of approximately 400 ms (Cansino, 2009). The dysfunction of the hippocampus due to the aging process is associated with impaired recollection and familiarity of episodic memory, two forms of episodic memory retrieval (Cansino, 2009; Dickerson & Eichenbaum, 2010; Robitsek, Fortin, Koh, Gallagher, & Eichenbaum, 2008; St-Laurent, Abdi, Burianova, & Grady, 2011). Impaired recollection of episodic memory was demonstrated by poor performance on the memory test which indicated that humans start to decline in episodic memory recollection at the age of 31years with a rate of being unable to recall the source of one item approximately per two years of life (Cansino, 2009).

In addition to age-related declines in recollection of episodic memory, impaired familiarity of episodic memory is supported by poor performance on item recognition tests among older adults. With aging, persons gradually lose the ability to recognize previously seen items with a rate of forgetting approximately one item per four years. This deficit of memory familiarity may start as early as the age of 41years (Cansino, 2009). Because of the decline in both recollection and familiarity of episodic memory, older adults are less able to differentiate

re-experienced memory from newly encoded information (Cansino, 2009; Dickerson & Eichenbaum, 2010; Robitsek et al., 2008; St-Laurent et al., 2011).

In summary, older adults have deficits in episodic memory encoding and retrieval including recollection and familiarity. This decline in episodic memory starts at the age of 31 years and continues throughout a person's life span. Older adults have more difficulties building the association between different domains of information to construct a complete episodic memory, which impairs retrieval of this memory.

Sleep

The normal cycle of sleep.

Normal sleep consists of two different stages: REM sleep and NREM sleep, both of which are important for episodic memory formation. REM sleep is defined by low-voltage and high frequency in electroencephalography (EEG) patterns with rapid eye movement. NREM sleep is identified by an EEG pattern with a gradually slowing down of frequency and high voltage. There are four stages in NREM sleep: stage one, two, three, and four and stage three and four of NREM sleep are referred to as SWS. Together, during nocturnal sleep, REM and NREM sleep construct a sleep cycle which lasts around 90 minutes in the first cycle and 100 to 120 minutes in the final cycle during nocturnal sleep. Generally, 80% of total sleep time occupies in NREM sleep and the remaining 20% belongs to REM sleep in human adults (Guilleminault & Kreutzer, 2003).

The neurotransmitters involved in sleep.

The sleep-wake cycle is associated with the oscillation of several neurotransmitters (i.e., acetylcholine, serotonin, norepinephrine, histamine, dopamine, orexin (hypocretin), gamma-Aminobutyric acid (GABA), glutamate, and adenosine), each of which is important for

consolidation of episodic memory. The roles of these neurotransmitters in consolidation of episodic memory will be discussed in the section "Sleep and episodic memory consolidation".

The master for controlling the circadian rhythmicity.

In addition to oscillation of neurotransmitters, sleep-wake is mainly regulated by the SCN which is located in the anterior hypothalamus. The neurons of the SCN can be divided into two groups: arginine vasopressin-expressing neurons and vasoactive intestinal polypeptide-expressing neurons based on the secreted neurotransmitter (Hofman & Swaab, 2006; Wu & Swaab, 2007). The vasoactive intestinal polypeptide-expressing neurons mainly receive the inputs of the retinohypothalamic tract that are important for the entrainment of light stimuli. The arginine vasopressin-expressing neurons of the SCN not only regulate rhythmic activity of the SCN but also control the circadian rhythmicity in other brain regions by their neural outputs (Wu & Swaab, 2007). Through the indirect connection between the SCN and the other brain regions, the SCN modulates the human's circadian rhythmicity including sleep-wake cycle. The regulation of the SCN on the circadian rhythm is through controlling the secretion of melatonin in the pineal gland (Morris, Aeschbach, & Scheer, 2012; Wu & Swaab, 2007), the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary gland to promote the secretion of cortisol from the adrenal cortex (Morris et al., 2012), the secretion of GABA in the ventrolateral preoptic nucleus and the release of orexin neurons of the lateral hypothalamus (Saper, Scammell, & Lu, 2005).

Sleep disturbances in older adults.

The neural mechanism of sleep disturbances in older adults.

The degeneration of suprachiasmatic nucleus (SCN) and circadian rhythm.

The mechanism of sleep disturbances in older adults is associated with the degeneration of the SCN system in the hypothalamus (Hofman & Swaab, 2006; Wu & Swaab, 2007). There are three main age-related changes in the SCN that contribute to sleep disturbances: decrease in the circadian amplitude of arginine vasopressin-expressing neurons of the SCN (Cajochen, Munch, Knoblauch, Blatter, & Wirz-Justice, 2006), calcification of the pineal gland which is controlled by the SCN to regulate sleep-wake cycle, and dysfunction of neuropathy of the SCN due to aging (Wu & Swaab, 2007). Decrease in the circadian amplitude of arginine vasopressin-expressing neurons can impair the control of rhythmic changes of the human body including the sleep-wake cycle (Cajochen et al., 2006). Additionally, the age-related calcification of the pineal gland can reduce the secretion of melatonin, particularly in the night-time, that contributes to sleep disturbances. Additionally, age-related dysfunction of the neuropathy, which can transmit inputs from external environment to the SCN, is associated with sleep disturbances. Another age-related change is the decreasing capacity of lens of the eyes to transmit light stimuli to the SCN because of aging degeneration or other pathological changes in the lens (e.g., catatract), which are related to sleep disturbances in older adults (Wu & Swaab, 2007).

The hyperactivity of hypothalamo-pituitory-adrenal axis due to aging process.

During the aging process, the hypothalamo-pituitory-adrenal axis becomes hyperactive, which contributes to sleep disturbances in older adults. This hyperactivity can be attributed to the decreases in melatonin and exogenous growth-hormone-releasing hormone. The age-related hyperactivity of the hypothalamo-pituitory-adrenal axis is characterized by an increase in

evening cortisol secretion and an advance and elevation of nocturnal nadir of it. These changes in cortisol can induce fragmented sleep at night and a decrease in SWS (Buckley & Schatzberg, 2005).

Other factors related to sleep disturbances in the older adults.

Some behavioral and environmental factors contribute to sleep disturbances in older adults. For instance, some behavioral factors (e.g., poor sleep hygiene, dietary habits, excessive daytime napping and nocturia) may be related to difficulty in falling asleep or causing an increase in fragmented sleep in older adults. The environmental factors (e.g., noise) can influence nocturnal sleep quality. Apart from behavioral and environmental factors, studies have shown that the higher prevalence of some chronic diseases in older adults contributes to poor nocturnal sleep and sleep may be disrupted by other sleep disorders (e.g., REM sleep behavior disorder, periodic leg movement, restless legs syndrome, and sleep-related respiratory disorder) (Edwards et al., 2010).

Sleep and Episodic Memory

Sleep and episodic memory consolidation.

Sleep plays a critical role in consolidating memory. Both sleep stages, REM and NREM sleep, are necessary for memory consolidation, particularly hippocampus-dependent memory such as episodic memory (Poe, Walsh, & Bjorness, 2010; Rauchs, Desgranges, Foret, & Eustache, 2005).

The consolidation of different types of memory occurs in different sleep stages. Generally, NREM sleep tends to be, but is not exclusively involved in the consolidation of declarative memory, while REM sleep tends to be, but is not exclusively involved, in the consolidation of non-declarative memory (Marshall & Born, 2007; Poe et al., 2010). However, a

deeper and more detailed investigation suggests a more complex picture. Studies have shown that consolidation of episodic memory is related to not only REM sleep but also NREM sleep, which can be explained by the co-activation of the hippocampus and the associated neocortical areas during sleep (Rauchs et al., 2005).

The role of NREM sleep in episodic memory consolidation.

NREM sleep, specifically SWS, plays a critical role in hippocampus-dependent memory consolidation including episodic memory. During SWS, the neurotransmitter changes (e.g., lowest level of cortisol and acetycholine) can promote the consolidation of newly encoded episodic memory which is acquired during wakefulness (Payne, Ellenbogen, Walker, & Stickgold, 2008). Evidence suggests that the circadian suppression of cortisol during the SWS is beneficial for consolidation of hippocampus-dependent memory, particularly episodic memory (Payne et al., 2008). In addition to lower level of cortisol, during SWS in which the level of acetylcholine is at its lowest, the newly encoded information is allowed to flow back to the associated neocortical areas from the hippocampus via the deeper layer of the entorhinal cortex to reactivate the associated brain regions of episodic memory. Lower level of acetylcholine during SWS may prevent the inputs of information from other brain regions to promote the replay of neural activity of newly encoded memory between the hippocampus and the associated neocortical areas (Payne et al., 2008; Rauchs et al., 2005). This co-activation between the hippocampus and associated neocortex, referred to as hippocampus-neocortical dialogue, is important for synaptic plasticity, particularly in the late stage of long-term potentiation (LTP), which is the neural basis of episodic memory consolidation. During SWS, the early stage of LTP which only lasts 4 to 6 hours is converted into late stage of LTP which lasts longer and is more

resistant to disturbance. This changes of LTP can be attributed to the completion of synthesis of the necessary protein for the changes of synapse (Poe et al., 2010).

In addition to the stage 3 and 4 of NREM sleep, which is also named SWS, stage two of NREM sleep is involved in episodic memory consolidation. According to the study of van der Helm, Gujar, Nishida, and Walker (2011), the performance of episodic memory was positively correlated with the time of stage two NREM sleep and the number of spindle waves of stage two of NREM sleep during nap time (van der Helm et al., 2011). During stage two of NREM sleep which is characterized by spindles or theta/spindles complex waves, the co-activation between the hippocampal CA1 field and the subiculum and the prefrontal lobe is related to the bidirectional synaptic plasticity [i.e., LTP and long-tern depression (LTD)] in the prefrontal cortex, which is induced by the hippocampus via the interaction between this brain region and the prefrontal cortex (Poe et al., 2010).

The role of REM sleep in episodic memory consolidation.

In addition to NREM sleep, REM sleep is important for episodic memory consolidation. During REM sleep, a change in neurotransmitters occurs, including a decrease of norepinephrine and serotonin. This process can facilitate bidirectional synaptic plasticity of LTP and LTD in the hippocampus, which form the basis of neurological changes in episodic memory consolidation. In particular, both norepinephrine and serotonin can promote LTP and inhibit LTD in the hippocampus which is very important for episodic memory consolidation (Poe et al., 2010). Thus, the reduction of norepinephrine and serotonin during REM sleep can provide an opportunity to induce LTD and recycle the limited synapses in the hippocampus (Best, Diniz Behn, Poe, & Booth, 2007; Poe et al., 2010).

In addition to neurotransmitters changes, brain waves changes including the ponto-geniculo-occipital wave and the oscillation of theta waves during REM sleep are important for episodic memory consolidation. The ponto-geniculo-occipital wave can increase during REM sleep after intensive daily learning and its elevation is associated with episodic memory consolidation in REM sleep (Poe et al., 2010). The oscillation of theta waves is related to bidirectional synaptic plasticity in the hippocampus which forms the basis of neurological changes in episodic memory consolidation (Rauchs et al., 2005). Additionally, during REM sleep, the theta wave allows the newly encoded information to flow from the associated neocortical area to the hippocampus via the superior layer of the entorhinal cortex, which is beneficial for strengthening the memory trace to promote episodic memory consolidation (Payne et al., 2008).

In summary, both REM and NREM sleep are critical for the consolidation of episodic memory. Total sleep deprivation including NREM and REM sleep for 96 hours could reduce neurogenesis in the hippocampus by 40% (Poe et al., 2010) while REM sleep deprivation can reduce cell proliferation in the hippocampus by 63%, both of which can affect memory consolidation (Meerlo, Mistlberger, Jacobs, Heller, & McGinty, 2009). Thus, intact function of episodic memory highly relies on complete sleep-wake cycle with sufficient and complete REM and NREM sleep.

Sleep and episodic memory encoding.

In addition to episodic memory consolidation, sleep is involved in memory encoding, including episodic memory. To explore this relationship, a study investigated the role of sleep before a learning task by imposing on a 36-hour sleep deprivation period and asking participants to perform a learning task. The results showed that sleep deprivation was associated with 40% of reduction in memory retention, indicating an impairment of memory encoding (Walker, 2008).

According to results of functional magnetic resonance imaging studies, after total sleep deprivation, the activity of the medial temporal lobe, including the hippocampus, is significantly reduced, while the activity of the prefrontal cortex increases. These results suggest that a reduced capacity for memory encoding is possibly associated with bidirectional changes: failure of the medial temporal lobe to process new information and overcompensation by the prefrontal cortex (Walker, 2008).

The effect of sleep deprivation on episodic memory in humans.

Sleep deprivation in young adults can influence the function of episodic memory. Several studies have indicated that total sleep deprivation in young adults (age:18-34) is associated with a deficit in episodic memory. Young adults, who experienced 7 to 35 hours of total sleep deprivation after learning tasks, performed significantly more poorly on episodic memory tests on the next day as compared to the young adults who had normal sleep (Drosopoulos, Windau, Wagner, & Born, 2007; Ellenbogen, Hulbert, Jiang, & Stickgold, 2009; Fenn et al., 2009; Hu, Stylos-Allan, & Walker, 2006; Lahl & Pietrowsky, 2007; Yoo, Hu, Gujar, Jolesz, & Walker, 2007). In addition to total sleep deprivation, partial sleep deprivation (e.g. REM sleep or SWS) after a learning task contributed to a deficit in episodic memory among young adults (age:18-26) (Ficca, Lombardo, Rossi, & Salzarulo, 2000; Rauchs et al., 2004).

The Roles of Attention, Executive Function, Cognitive Reserve, and Depressive Symptoms

Attention

Attention is a complex cognitive process that can be described in terms of four dimensions: arousal, sustained attention, divided attention, and selective attention. Arousal refers to a state of alertness, responsiveness, or wakefulness. Sustained attention, known as vigilance, involves the ability to sustain attention over a period of time. Divided attention refers to the

capacity to engage in more than one stimulus or task simultaneously. Selective attention describes the ability to focus attention on one stimulus or task, while suppressing the potential disturbance from other competing stimuli (Hodges, 2007). According to the Dual Attentional Process hypothesis, attention involves two processes: top-down or goal-driven allocation of attention, supported by dorsal posterior parietal cortex and reflexive attention, supported by ventral posterior parietal cortex (Hutchinson, Uncapher, & Wagner, 2009).

Attention and sleep.

Attention can be influenced by sleep. After sleep deprivation, individuals demonstrated poor attention processes such as decreased ability to shift attention to new stimuli, greater likelihood of losing attention to repeated stimuli, decreased reactive strength to stimuli, and difficulty in ignoring distractions (McCarthy & Waters, 1997). In addition to these effects of sleep deprivation, daytime sleepiness and a decreased level of arousal due to total sleep deprivation can impair attention performances in terms of longer reaction time and incorrect responses (Goel, Rao, Durmer, & Dinges, 2009; Lim & Dinges, 2008). Sleep restriction (4-hour total sleep time) affects attention and is associated with more errors on attention tests (Stenuit & Kerkhofs, 2008). Daytime sleepiness due to sleep disturbances was shown to contribute to difficulty in concentrating and focusing attention on stimuli in a study of 1,026 older adults (Ohayon & Vecchierini, 2002). In contrast to older adults who have sleep problems, older adults who have good sleep quality perform better on attention tests (Nebes et al., 2009). Older adults with shorter sleep time $\leq$ 5 hours and taking sleep medicine had more difficulty in attention-concentration (Ohayon & Vecchierini, 2002).

Attention and episodic memory.

Attention may play a role in the formation of episodic memory. Both attention processes (top-down allocation of attention and reflexive attention) are involved in formation of episodic memory, particularly episodic retrieval. For instance, top-down allocation of attention is engaged to allocate attention toward relevant cues needed to retrieve stored episodic memory, while reflexive attention is involved in the capture of attention related to retrieve episodic memory. The function of attention is supported by the dorsal and ventral posterior parietal cortex. Both of these two brain regions are involved in episodic memory formation (Hutchinson et al., 2009). Impaired attention may influence formation of episodic memory (Cole & Richards, 2005).

Executive function.

Executive function refers to the complex cognitive abilities involved in the control and coordination of voluntary behavior to achieve a goal (Goel et al., 2009). This function includes the ability to focus attention by ignoring distractions, planning and arranging thought and behavior, inhibiting inappropriate thoughts and behavior, constructing abstract concepts, updating new information into a related memory structure, and thinking more flexibly and variously. Executive function is dependent on the interaction between different brain regions and is mainly controlled by the prefrontal cortex (Killgore, 2010).

Executive function and sleep.

Executive function is associated with sleep through its dependence on the functioning of the prefrontal cortex. The prefrontal cortex is more active during waking hours and requires sleep, particularly SWS, to restore the function of the prefrontal cortex. This was shown in a study by Harrison et al. (2000) that found that a 36-hour total sleep deprivation contributed to dysfunction of the prefrontal cortex (Harrison et al., 2000) and led to poor performance in

complex executive function (Harrison & Horne, 1999). Fragmentation of sleep-wake rhythm has been significantly and negatively correlated with executive function performance (Oosterman et al., 2009).

Executive function and episodic memory.

The prefrontal cortex plays a critical role in episodic memory processes, particularly in encoding and retrieval of memory. The prefrontal cortex is associated with efficient memory encoding and is considered to be the trigger of episodic memory retrieval (Brand & Markowitsch, 2008). Deficits in the prefrontal cortex may influence episodic memory function. This influence was explored in a study by Parks et al. (2011) (n=422) who found that the degree of white matter hyperintensities across the whole brain was negatively correlated with the performance of executive function. However, once the effect of executive function was removed statistically, these two variables were not correlated with each other. The relationship between hippocampal volume and episodic memory became very weak when the executive function was low. These results suggested that the influences of white matter hyperintensities across the whole brain and of hippocampal volume on episodic memory were indirect, and mediated significantly by the prefrontal cortex and executive function (Parks et al., 2011a).

Cognitive reserve.

Cognitive reserve is defined as the ability to optimize or maximize cognitive performance, including episodic memory, by recruiting different neural networks or utilizing the original neural network to more efficiently respond to greater cognitive demands (Stern, 2002). In other words, cognitive reserve is the utilization of an alternative cognitive strategy. Individuals with more cognitive reserve can tolerate higher levels of brain dysfunction than individuals with less cognitive reserve before functional impairment becomes apparent (Stern,

2002). Cognitive reserve mediates the effect of damage to or pathological changes of the brain on the demonstration of symptoms or change of function (Stern, 2009). The concept of cognitive reserve may explain why higher levels of intelligence or higher educational and occupational status are good predictors for which individuals can maintain normal function under sustained brain damage (e.g., Alzheimer's disease or aging) (Stern, 2002).

Cognitive reserve and sleep.

Cognitive reserve may be influenced by poor sleep due to negative neuroplasticity. Negative neuroplasticity refers to harmful morphological changes in the brain (i.e., reduced or weaker dendritic connection between neurons, a reduction of brain volume, and decreased secretion of neutrophic factors). Poor sleep may promote negative neuroplasticity and in turn lead to a decline in cognitive reserve (Vance et al., 2010).

Cognitive reserve and episodic memory.

Considering the role of cognitive reserve in neural network and cognitive processes, it is reasonable to infer that cognitive reserve is associated with cognitive performance including episodic memory. This was demonstrated in a study by Zimmerman et al. (2012) which found older adults with a higher cognitive reserve, as determined by educational level, may be more resistive to the negative effect of sleep problems on executive function (Zimmerman et al., 2012). Based on these results, it is possible to infer that cognitive reserve may influence the effectiveness of episodic memory.

Depressive symptoms and sleep.

Sleep disturbances have been shown to be related to depressive symptoms. Several studies found that sleep disturbances including objective and subjective sleep characteristics were correlated with severity or number of depressive symptoms (Maglione et al., 2012; Paudel

et al., 2008). The studies by Paudel et al. (2008) and Maglione et al. (2012) found that compared to older adults who had fewer depressive symptoms, those who had more depressive symptoms had more objectively measured sleep disturbances (i.e., reduced sleep efficiency, increased sleep latency, longer fragmented sleep episodes, greater numbers of fragmented sleep episodes, and greater subjective sleep complaints (i.e., poor sleep quality and increased daytime sleepiness) (Maglione et al., 2012; Paudel et al., 2008).

The study by Nebes et al. (2009) found that compared to the older adults who had good sleep quality, those who had poor sleep quality had more depressive symptoms (Nebes et al., 2009). Depression is considered as a significant cause of chronic insomnia and insomnia is a frequent symptom of depression (Franzen & Buysse, 2008). In summary, sleep disturbances and depressive symptoms may be significantly correlated with each other bi-directionally.

Depressive symptoms and episodic memory.

Depressive symptoms have been associated with episodic memory in older adults. A study by Panza et al. (2009) found that greater depressive symptoms were significantly correlated with poor performance on episodic memory tests including immediate and delayed recall. Furthermore, depressive symptoms were significantly associated with an accelerated rate of episodic memory decline over the course of 3.5 years in older adults (Panza et al., 2009). A study by Beaudreau and O'Hara (2009) indicated that an increased number of depressive symptoms were significantly correlated with poor episodic memory performance in this population (Beaudreau & O'Hara, 2009). Moreover, the study by González et al. (2008) found that increased depressive symptoms were correlated with decline of verbal episodic learning and delayed recall score (Gonzalez et al., 2008). To summarize, depressive symptoms were significantly related to the deficits of episodic memory.

Summary

In summary, theoretical perspectives have been used to describe the mechanisms underlying the relationship between age-related declines in episodic memory and sleep disturbances. The critical role of sleep in the consolidation and encoding of episodic memory has been demonstrated in previous studies. Total and partial sleep deprivation may contribute to decline in episodic memory. Given the evidence, it is reasonable to infer that sleep disturbances may be associated with episodic memory decline. In older adults, age-related sleep disturbances and declines in episodic memory are common problems. In addition to sleep disturbances, other related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve) may affect the relationship between sleep disturbances and episodic memory. The theoretical framework based on this theoretical perspective is shown in Figure 1.1. This study hypothesizes that sleep disturbances in older adults are associated with declines in episodic memory and other related factors mediate or moderate this relationship. To examine this hypothesis, this relationship between sleep disturbances and episodic memory in older adults is investigated together with an exploration of possible mediating or moderating effect of these related factors in this study. The results of this study may be helpful for developing effective nursing interventions directed at helping older adults prevent declines in episodic memory by improving sleep.

References

Abel, T., & Lattal, K. M. (2001). Molecular mechanisms of memory acquisition, consolidation and retrieval. *Current Opinion in Neurobiology, 11*(2), 180-187.

Algase, D. L., & Whall, A. F. (1993). Rosemary Ellis' views on the substantive structure of nursing. *Image-the Journal of Nursing Scholarship, 25*(1), 69-72.

Aly, M., & Moscovitch, M. (2010). The effects of sleep on episodic memory in older and younger adults. *Memory, 18*(3), 327-334. doi: 10.1080/09658211003601548

Backhaus, J., Born, J., Hoeckesfeld, R., Fokuhl, S., Hohagen, F., & Junghanns, K. (2007). Midlife decline in declarative memory consolidation is correlated with a decline in slow wave sleep. *Learning & Memory, 14*(5), 336-341. doi: 10.1101/lm.470507

Beaudreau, S. A., & O'Hara, R. (2009). The association of anxiety and depressive symptoms with cognitive performance in community-dwelling older adults. *Psychology and Aging, 24*(2), 507-512. doi: 10.1037/a0016035

Beaunieux, H., Hubert, V., Pitel, A. L., Desgranges, B., & Eustache, F. (2009). Episodic memory deficits slow down the dynamics of cognitive procedural learning in normal ageing. *Memory, 17*(2), 197-207. doi: 10.1080/09658210802212010

Best, J., Diniz Behn, C., Poe, G. R., & Booth, V. (2007). Neuronal models for sleep-wake regulation and synaptic reorganization in the sleeping hippocampus. *Journal of Biological Rhythms, 22*(3), 220-232. doi: 10.1177/0748730407301239

Bonanni, E., Maestri, M., Tognoni, G., Fabbrini, M., Nucciarone, B., Manca, M. L., . . . Murri, L. (2005). Daytime sleepiness in mild and moderate Alzheimer's disease and its relationship with cognitive impairment. *Journal of Sleep Research, 14*(3), 311-317. doi: 10.1111/j.1365-2869.2005.00462.x

Brand, M., & Markowitsch, H. J. (2008). Chapter 3.5 The role of the prefrontal cortex in episodic memory. *Handbook of behavioral neuroscience: Vol.18.Handbook of episodic memory, 18,* 317-619. doi: 10.1016/s1569-7339(08)00218-x

Buckley, T. M., & Schatzberg, A. F. (2005). Aging and the role of the HPA axis and rhythm in sleep and memory-consolidation. *The American Journal of Geriatric Psychiatry, 13*(5), 344-352. doi: 10.1176/appi.ajgp.13.5.344

Budson, A. E., & Price, B. H. (2005). Memory dysfunction. *The New England Journal of Medicine, 352*(7), 692-699. doi: 10.1056/NEJMra041071

Burton, C. L., Strauss, E., Hultsch, D. F., & Hunter, M. A. (2006). Cognitive functioning and everyday problem solving in older adults. *The Clinical Neuropsychologist, 20*(3), 432-452. doi: 10.1080/13854040590967063

Cajochen, C., Munch, M., Knoblauch, V., Blatter, K., & Wirz-Justice, A. (2006). Age-related changes in the circadian and homeostatic regulation of human sleep. *Chronobiology International, 23*(1-2), 461-474. doi: 10.1080/07420520500545813

Cansino, S. (2009). Episodic memory decay along the adult lifespan: a review of behavioral and neurophysiological evidence. *International Journal of Psychophysiology, 71*(1), 64-69. doi: 10.1016/j.ijpsycho.2008.07.005

Cochrane, A., Robertson, I. H., & Coogan, A. N. (2012). Association between circadian rhythms, sleep and cognitive impairment in healthy older adults: an actigraphic study. *Journal of Neural Transmission, 119*(10), 1233-1239. doi: 10.1007/s00702-012-0802-2

Cole, C. S., & Richards, K. C. (2005). Sleep and cognition in people with Alzheimer's disease. *Issue in Mental Health Nursing, 26*(7), 687-698. doi: 10.1080/01612840591008258

Dickerson, B. C., & Eichenbaum, H. (2010). The episodic memory system: neurocircuitry and disorders. *Neuropsychopharmacology, 35*(1), 86-104. doi: 10.1038/npp.2009.126

Drosopoulos, S., Windau, E., Wagner, U., & Born, J. (2007). Sleep enforces the temporal order in memory. *PLoS One, 2*(4), e376. doi: 10.1371/journal.pone.0000376

Edwards, B. A., O'Driscoll, D. M., Ali, A., Jordan, A. S., Trinder, J., & Malhotra, A. (2010). Aging and sleep: physiology and pathophysiology. *Seminars in Respiratory and Critical Care Medicine, 31*(5), 618-633. doi: 10.1055/s-0030-1265902

Ellenbogen, J. M., Hulbert, J. C., Jiang, Y., & Stickgold, R. (2009). The sleeping brain's influence on verbal memory: boosting resistance to interference. *PLoS One, 4*(1), e4117. doi: 10.1371/journal.pone.0004117

Ensrud, K. E., Blackwell, T. L., Redline, S., Ancoli-Israel, S., Paudel, M. L., Cawthon, P. M., . . . Osteoporotic Fractures in Men Study, G. (2009). Sleep disturbances and frailty status in older community-dwelling men. *Journal of the American Geriatrics Society, 57*(11), 2085-2093. doi: 10.1111/j.1532-5415.2009.02490.x

Espiritu, J. R. (2008). Aging-related sleep changes. *Clinics in Geriatric Medicine, 24*(1), 1-14, v. doi: 10.1016/j.cger.2007.08.007

Fenn, K. M., Gallo, D. A., Margoliash, D., Roediger, H. L., & Nusbaum, H. C. (2009). Reduced false memory after sleep. *Learning & Memory, 16*(9), 509-513. doi: 10.1101/lm.1500808

Ferrie, J. E., Shipley, M. J., Akbaraly, T. N., Marmot, M. G., Kivimaki, M., & Singh-Manoux, A. (2011). Change in sleep duration and cognitive function: findings from the Whitehall II Study. *Sleep, 34*(5), 565-573.

Ficca, G., Lombardo, P., Rossi, L., & Salzarulo, P. (2000). Morning recall of verbal material depends on prior sleep organization. *Behavioural Brain Research, 112*(1-2), 159-163.

Fogel, J. F., Hyman, R. B., Rock, B., & Wolf-Klein, G. (2000). Predictors of hospital length of stay and nursing home placement in an elderly medical population. *Journal of the American Medical Directors Association, 1*(5), 202-210.

Foley, D. J., Monjan, A. A., Brown, S. L., Simonsick, E. M., Wallace, R. B., & Blazer, D. G. (1995). Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep, 18*(6), 425-432.

Fotuhi, M., Do, D., & Jack, C. (2012). Modifiable factors that alter the size of the hippocampus with ageing. *Nature Reviews.Neurology, 8*(4), 189-202. doi: 10.1038/nrneurol.2012.27

Franzen, P. L., & Buysse, D. J. (2008). Sleep disturbances and depression: risk relationships for subsequent depression and therapeutic implications. *Dialogues in Clinical Neuroscience, 10*(4), 473-481.

Fuller, S. S. (1978). Holistic man and the science and practice of nursing. *Nursing Outlook, 26*(11), 700-704.

Gamaldo, A. A., Allaire, J. C., & Whitfield, K. E. (2008). The Relationship Between Reported Problems Falling Asleep and Cognition Among African American Elderly. *Research on Aging, 30*(6), 752-767. doi: 10.1177/0164027508322576

Goel, N., Rao, H., Durmer, J. S., & Dinges, D. F. (2009). Neurocognitive consequences of sleep deprivation. *Seminars in Neurology, 29*(4), 320-339. doi: 10.1055/s-0029-1237117

Goldberg, T. E., Koppel, J., Keehlisen, L., Christen, E., Dreses-Werringloer, U., Conejero-Goldberg, C., . . . Davies, P. (2010). Performance-based measures of everyday function in mild cognitive impairment. *American Journal of Psychiatry, 167*(7), 845-853. doi: 10.1176/appi.ajp.2010.09050692

Gonzalez, H. M., Bowen, M. E., & Fisher, G. G. (2008). Memory decline and depressive symptoms in a nationally representative sample of older adults: the Health and Retirement Study (1998-2004). *Dementia and Geriatric Cognitive Disorders, 25*(3), 266-271. doi: 10.1159/000115976

Guilleminault, C., & Kreutzer, M. L. (2003). Normal sleep. In M. Billiard (Ed.), *Sleep: Physiology, Investigations, and Medicine* (pp. 3-9). New York, NY: Kluwer Academic/Plenum Publisher.

Haimov, I. (2006). Association between memory impairment and insomnia among older adults. *European Journal of Ageing, 3*(2), 107-115. doi: 10.1007/s10433-006-0026-0

Harrison, Y., & Horne, J. A. (1999). One night of sleep loss impairs innovative thinking and flexible decision making. *Organizational Behavior and Human Decision Processes, 78*(2), 128-145.

Harrison, Y., Horne, J. A., & Rothwell, A. (2000). Prefrontal neuropsychological effects of sleep deprivation in young adults--a model for healthy aging? *Sleep, 23*(8), 1067-1073.

Hart, R. P., Morin, C. M., & Best, A. M. (1995). Neuropsychological performance in elderly insomnia patients. *Aging, Neuropsychology, and Cognition, 2*(4), 268-278.

Hodges, J. R. (2007). *Cognitive assessment for clinicians*. Oxford, NY: Oxford University Press.

Hofman, M. A., & Swaab, D. F. (2006). Living by the clock: the circadian pacemaker in older people. *Aging Research Reviews, 5*(1), 33-51. doi: 10.1016/j.arr.2005.07.001

Hornung, O. P., Regen, F., Danker-Hopfe, H., Schredl, M., & Heuser, I. (2007). The relationship between REM sleep and memory consolidation in old age and effects of cholinergic medication. *Biological Psychiatry, 61*(6), 750-757. doi: 10.1016/j.biopsych.2006.08.034

Hu, P., Stylos-Allan, M., & Walker, M. P. (2006). Sleep facilitates consolidation of emotional declarative memory. *Psychological Science, 17*(10), 891-898. doi: 10.1111/j.1467-9280.2006.01799.x

Hutchinson, J. B., Uncapher, M. R., & Wagner, A. D. (2009). Posterior parietal cortex and episodic retrieval: convergent and divergent effects of attention and memory. *Learn Mem, 16*(6), 343-356. doi: 10.1101/lm.919109

Killgore, W. D. (2010). Effects of sleep deprivation on cognition. *Prog Brain Res, 185*, 105-129. doi: 10.1016/B978-0-444-53702-7.00007-5

Kronholm, E., Sallinen, M., Suutama, T., Sulkava, R., Era, P., & Partonen, T. (2009). Self-reported sleep duration and cognitive functioning in the general population. *Journa of Sleep Research, 18*(4), 436-446. doi: 10.1111/j.1365-2869.2009.00765.x

Lahl, O., & Pietrowsky, R. (2007). The long range effect of sleep on episodic memory. *Sleep and Hypnosis, 9*(1), 24-29.

Lavery, L. L., Dodge, H. H., Snitz, B., & Ganguli, M. (2009). Cognitive decline and mortality in a community-based cohort: the Monongahela Valley Independent Elders Survey. *Journal of the American Geriatrics Society, 57*(1), 94-100. doi: 10.1111/j.1532-5415.2008.02052.x

Lee, H. B., Kasper, J. D., Shore, A. D., Yokley, J. L., Black, B. S., & Rabins, P. V. (2006). Level of cognitive impairment predicts mortality in high-risk community samples: the memory and medical care study. *Journal of neuropsychiatry and clinical neurosciences, 18*(4), 543-546. doi: 10.1176/appi.neuropsych.18.4.543

Lim, J., & Dinges, D. F. (2008). Sleep deprivation and vigilant attention. *Ann N Y Acad Sci, 1129*, 305-322. doi: 10.1196/annals.1417.002

Loerbroks, A., Debling, D., Amelang, M., & Sturmer, T. (2010). Nocturnal sleep duration and cognitive impairment in a population-based study of older adults. *International Journal of Geriatric Psychiatry, 25*(1), 100-109. doi: 10.1002/gps.2305

Maglione, J. E., Ancoli-Israel, S., Peters, K. W., Paudel, M. L., Yaffe, K., Ensrud, K. E., & Stone, K. L. (2012). Depressive symptoms and subjective and objective sleep in community-dwelling older women. *Journal of the American Geriatrics Society, 60*(4), 635-643. doi: 10.1111/j.1532-5415.2012.03908.x

Maki, Y., Yamaguchi, T., Yamagami, T., Murai, T., Hachisuka, K., Miyamae, F., . . . Yamaguchi, H. (2014). The impact of subjective memory complaints on quality of life in community-dwelling older adults. *Psychogeriatrics, 14*(3), 175-181. doi: 10.1111/psyg.12056

Manocchia, M., Keller, S., & Ware, J. E. (2001). Sleep problems, health-related quality of life, work functioning and health care utilization among the chronically ill. *Qual Life Res, 10*(4), 331-345.

Marshall, L., & Born, J. (2007). The contribution of sleep to hippocampus-dependent memory consolidation. *Trends in Cognitive Sciences, 11*(10), 442-450. doi: 10.1016/j.tics.2007.09.001

Martin, J. L., Fiorentino, L., Jouldjian, S., Josephson, K. R., & Alessi, C. A. (2010). Sleep quality in residents of assisted living facilities: effect on quality of life, functional status, and depression. *Journal of the American Geriatrics Society, 58*(5), 829-836. doi: 10.1111/j.1532-5415.2010.02815.x

Mazzoni, G., Gori, S., Formicola, G., Gneri, C., Massetani, R., Murri, L., & Salzarulo, P. (1999). Word recall correlates with sleep cycles in elderly subjects. *Journal of Sleep Research, 8*(3), 185-188.

McCarthy, M. E., & Waters, W. F. (1997). Decreased attentional responsivity during sleep deprivation: orienting response latency, amplitude, and habituation. *Sleep, 20*(2), 115-123.

Meerlo, P., Mistlberger, R. E., Jacobs, B. L., Heller, H. C., & McGinty, D. (2009). New neurons in the adult brain: the role of sleep and consequences of sleep loss. *Sleep Medicine Reviews, 13*(3), 187-194. doi: 10.1016/j.smrv.2008.07.004

Merritt, P., Hirshman, E., Zamani, S., Hsu, J., & Berrigan, M. (2006). Episodic representations support early semantic learning: evidence from midazolam induced amnesia. *Brain and Cognition, 61*(2), 219-223. doi: 10.1016/j.bandc.2005.12.001

Morris, C. J., Aeschbach, D., & Scheer, F. A. (2012). Circadian system, sleep and endocrinology. *Molecular and Cellular Endocrinology, 349*(1), 91-104. doi: 10.1016/j.mce.2011.09.003

Moscovitch, M., Winocur, G., Ryan, L., & Nadel, L. (2008). Chapter 3.1 Functional neuroanatomy of remote, episodic memory. *Handbook of behavioral neuroscience: Vol.18.Handbook of episodic memory, 18*, 239-269. doi: 10.1016/s1569-7339(08)00214-2

National Institute of Nursing Research (2011), Bringing Science to Life:NINR Strategic plan. 09 April 2015. Retrived from https://www.ninr.nih.gov/sites/www.ninr.nih.gov/files/ninr-strategic-plan-2011.pdf

Nebes, R. D., Buysse, D. J., Halligan, E. M., Houck, P. R., & Monk, T. H. (2009). Self-reported sleep quality predicts poor cognitive performance in healthy older adults. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences 64*(2), 180-187. doi: 10.1093/geronb/gbn037

Ohayon, M. M., & Vecchierini, M. F. (2002). Daytime sleepiness and cognitive impairment in the elderly population. *Archives of Internal Medicine, 162*(2), 201-208.

Oosterman, J. M., van Someren, E. J., Vogels, R. L., Van Harten, B., & Scherder, E. J. (2009). Fragmentation of the rest-activity rhythm correlates with age-related cognitive deficits. *Journal of Sleep Research, 18*(1), 129-135. doi: 10.1111/j.1365-2869.2008.00704.x

Panza, F., D'Introno, A., Colacicco, A. M., Capurso, C., Del Parigi, A., Caselli, R. J., . . . Solfrizzi, V. (2009). Temporal relationship between depressive symptoms and cognitive impairment: the Italian Longitudinal Study on Aging. *Journal of Alzheimer's Disease, 17*(4), 899-911. doi: 10.3233/JAD-2009-1111

Parks, C. M., Iosif, A. M., Farias, S., Reed, B., Mungas, D., & DeCarli, C. (2011). Executive function mediates effects of white matter hyperintensities on episodic memory. *Neuropsychologia, 49*(10), 2817-2824. doi: 10.1016/j.neuropsychologia.2011.06.003

Paudel, M. L., Taylor, B. C., Diem, S. J., Stone, K. L., Ancoli-Israel, S., Redline, S., . . . Osteoporotic Fractures in Men Study, G. (2008). Association between depressive symptoms and sleep disturbances in community-dwelling older men. *Journal of the American Geriatrics Society, 56*(7), 1228-1235. doi: 10.1111/j.1532-5415.2008.01753.x

Payne, J. D., Ellenbogen, J. M., Walker, M. P., & Stickgold, R. (2008). The role of sleep in memory consolidation. In J. Byrne & H. L. Roediger (Eds.), *Learning and memory: A comprehensive reference* (Vol. 2. Cognitive psychology of memory, pp. 663-685). Oxford, UK: Elsevier.

Poe, G. R., Walsh, C. M., & Bjorness, T. E. (2010). Cognitive neuroscience of sleep. *Progress in Brain Research, 185*, 1-19. doi: 10.1016/B978-0-444-53702-7.00001-4

Pressler, S. J., Kim, J., Riley, P., Ronis, D. L., & Gradus-Pizlo, I. (2010). Memory dysfunction, psychomotor slowing, and decreased executive function predict mortality in patients with

heart failure and low ejection fraction. *Journal of Cardiac Failure, 16*(9), 750-760. doi: 10.1016/j.cardfail.2010.04.007

Rauchs, G., Bertran, F., Guillery-Girard, B., Desgranges, B., Kerrouche, N., Denise, P., . . . Eustache, F. (2004). Consolidation of strictly episodic memories mainly requires rapid eye movement sleep. *Sleep, 27*(3), 395-401.

Rauchs, G., Desgranges, B., Foret, J., & Eustache, F. (2005). The relationships between memory systems and sleep stages. *Journal of Sleep Research, 14*(2), 123-140. doi: 10.1111/j.1365-2869.2005.00450.x

Roberts, R. E., Shema, S. J., Kaplan, G. A., & Strawbridge, W. J. (2000). Sleep complaints and depression in an aging cohort: A prospective perspective. *American journal of psychiatry, 157*(1), 81-88.

Robitsek, R. J., Fortin, N. J., Koh, M. T., Gallagher, M., & Eichenbaum, H. (2008). Cognitive aging: a common decline of episodic recollection and spatial memory in rats. *The Journal of Neuroscience, 28*(36), 8945-8954. doi: 10.1523/JNEUROSCI.1893-08.2008

Saper, C. B., Scammell, T. E., & Lu, J. (2005). Hypothalamic regulation of sleep and circadian rhythms. *Nature, 437*(7063), 1257-1263. doi: 10.1038/nature04284

Schmutte, T., Harris, S., Levin, R., Zweig, R., Katz, M., & Lipton, R. (2007). The relation between cognitive functioning and self-reported sleep complaints in nondemented older adults: results from the Bronx aging study. *Behavioral Sleep Medicine, 5*(1), 39-56. doi: 10.1080/15402000709336725

Spencer, R. M., Gouw, A. M., & Ivry, R. B. (2007). Age-related decline of sleep-dependent consolidation. *Learning & Memory, 14*(7), 480-484. doi: 10.1101/lm.569407

Squire, L. R., & Kandel, E. R. (2009). *Memory: from Mind to Molecules*. Greenwood Village, CO: Roberts and Company Publishers.

St-Laurent, M., Abdi, H., Burianova, H., & Grady, C. L. (2011). Influence of aging on the neural correlates of autobiographical, episodic, and semantic memory retrieval. *Journal of Cognitive Neuroscience, 23*(12), 4150-4163. doi: 10.1162/jocn_a_00079

Stenuit, P., & Kerkhofs, M. (2008). Effects of sleep restriction on cognition in women. *Biological Psychology, 77*(1), 81-88. doi: 10.1016/j.biopsycho.2007.09.011

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society 8*(3), 448-460.

Stern, Y. (2009). Cognitive reserve. *Neuropsychologia, 47*(10), 2015-2028. doi: 10.1016/j.neuropsychologia.2009.03.004

Sutter, C., Zollig, J., Allemand, M., & Martin, M. (2012). Sleep quality and cognitive function in healthy old age: the moderating role of subclinical depression. *Neuropsychology, 26*(6), 768-775. doi: 10.1037/a0030033

Thorne, S., Canam, C., Dahinten, S., Hall, W., Henderson, A., & Kirkham, S. R. (1998). Nursing's metaparadigm concepts: disimpacting the debates. *Journal of Advanced Nursing*, 27(6), 1257-1268.

Tomaszewski Farias, S., Cahn-Weiner, D. A., Harvey, D. J., Reed, B. R., Mungas, D., Kramer, J. H., & Chui, H. (2009). Longitudinal changes in memory and executive functioning are associated with longitudinal change in instrumental activities of daily living in older adults. *The Clinical Neuropsychologist, 23*(3), 446-461. doi: 10.1080/13854040802360558

Tworoger, S. S., Lee, S., Schernhammer, E. S., & Grodstein, F. (2006). The association of self-reported sleep duration, difficulty in sleeping, and snoring with cognitive function in older women. *Alzheimer Disease and Associated Disorders, 20*(1), 41-48. doi: 10.1097/01.wad.0000201850.52707.80

van der Helm, E., Gujar, N., Nishida, M., & Walker, M. P. (2011). Sleep-dependent facilitation of episodic memory details. *PLoS One, 6*(11), e27421. doi: 10.1371/journal.pone.0027421

Van Der Werf, Y. D., Altena, E., Vis, J. C., Koene, T., & Van Someren, E. J. (2011). Reduction of nocturnal slow-wave activity affects daytime vigilance lapses and memory encoding but not reaction time or implicit learning. *Progress in Brain Research, 193*, 245-255. doi: 10.1016/B978-0-444-53839-0.00016-8

Vance, D. E., Roberson, A. J., McGuinness, T. M., & Fazeli, P. L. (2010). How neuroplasticity and cognitive reserve protect cognitive functioning. *Journal of Psychosocial Nursing and Mental Health Services, 48*(4), 23-30. doi: 10.3928/02793695-20100302-01

Walker, M. P. (2008). Cognitive consequences of sleep and sleep loss. *Sleep Medicine, 9 Suppl 1*, S29-34. doi: 10.1016/s1389-9457(08)70014-5

Westerberg, C. E., Lundgren, E. M., Florczak, S. M., Mesulam, M. M., Weintraub, S., Zee, P. C., & Paller, K. A. (2010). Sleep influences the severity of memory disruption in amnestic mild cognitive impairment: results from sleep self-assessment and continuous activity monitoring. *Alzheimer Disease and Associated Disorders, 24*(4), 325-333. doi: 10.1097/WAD.0b013e3181e30846

Westerberg, C. E., Mander, B. A., Florczak, S. M., Weintraub, S., Mesulam, M. M., Zee, P. C., & Paller, K. A. (2012). Concurrent impairments in sleep and memory in amnestic mild

cognitive impairment. *Journal of the International Neuropsychological Society, 18*(3), 490-500. doi: 10.1017/S135561771200001X

Wilson, J. K., Baran, B., Pace-Schott, E. F., Ivry, R. B., & Spencer, R. M. (2012). Sleep modulates word-pair learning but not motor sequence learning in healthy older adults. *Neurobiology of Aging, 33*(5), 991-1000. doi: 10.1016/j.neurobiolaging.2011.06.029

Wu, Y. H., & Swaab, D. F. (2007). Disturbance and strategies for reactivation of the circadian rhythm system in aging and Alzheimer's disease. *Sleep Medicine, 8*(6), 623-636. doi: 10.1016/j.sleep.2006.11.010

Xiao, Q., Keadle, S. K., Hollenbeck, A. R., & Matthews, C. E. (2014). Sleep duration and total and cause-specific mortality in a large US cohort: interrelationships with physical activity, sedentary behavior, and body mass index. *Am J Epidemiol, 180*(10), 997-1006. doi: 10.1093/aje/kwu222

Xu, L., Jiang, C. Q., Lam, T. H., Liu, B., Jin, Y. L., Zhu, T., . . . Thomas, G. N. (2011). Short or long sleep duration is associated with memory impairment in older Chinese: the Guangzhou Biobank Cohort Study. *Sleep, 34*(5), 575-580.

Yoo, S. S., Hu, P. T., Gujar, N., Jolesz, F. A., & Walker, M. P. (2007). A deficit in the ability to form new human memories without sleep. *Nature Neuroscience, 10*(3), 385-392. doi: 10.1038/nn1851

Zimmerman, M. E., Bigal, M. E., Katz, M. J., Brickman, A. M., & Lipton, R. B. (2012). Sleep onset/maintenance difficulties and cognitive function in nondemented older adults: the role of cognitive reserve. *Journal of the International Neuropsychological Society, 18*(3), 461-470. doi: 10.1017/S1355617711001901

Chapter Two

Sleep Disturbances and Episodic Memory in Older Adults: Systematic Literature Review

Abstract

Adults with sleep disorders have impaired episodic memory. However, older adults who suffer from sleep disturbances have received little attention. A systematic literature review was conducted to investigate the relationship between episodic memory and sleep disturbances among older adults. The databases searched included PubMed, CINAHL, PsycINFO, Medline, EBM-Reviews Cochrane. Results of the literature search produced 29 data-based publications. Six publications indicated that older adults with 6 to 8 hours of sleep time had better episodic memory than the adults with ≤ 5 hours and ≥ 9 hours sleep time. Self-reported sleep problems were negatively correlated with episodic memory and objectively measured sleep characteristics were significantly correlated with episodic memory among older adults. This raises the question of whether self-reported or objective measured sleep disturbances are more strongly associated with episodic memory and predictive of changes in memory performance, suggesting the need for further investigations for these knowledge gaps.

Keywords: Sleep, Sleep disturbances, Episodic memory, Aging

Introduction

Episodic memory involves learning, storing, and retrieving information about personal experience from daily life (Dickerson & Eichenbaum, 2010) and learning behavior (Beaunieux, Hubert, Pitel, Desgranges & Eustache, 2009; Merritt, Hirshman, Zamani, Hsu & Berrigan, 2006). Humans highly rely on personal experience to construct the self-world in the human mind and the concept of self (Squire & Kandel, 2009).

Older adults begin to lose efficiency in episodic memory, starting at about the third decade of life and continuing throughout life span (Cansino, 2009). Increasing impairment in episodic memory is associated with decrease in functional ability (i.e., activities of daily living and instrumental activities of daily living) (Goldberg et al., 2010; Burton, Strauss, Hultsch, & Hunter, 2006; Lee et al., 2006) and increased mortality among older adults with and without dementia (Lavery, Dodge, Snitz, & Ganguli, 2009). Thus, it is important to investigate the factors that contribute to dysfunction of episodic memory in older adults, one of which is sleep disturbances.

More than 50% of older adults complained of chronic sleep disturbances (Foley, Monjan, Brown, & Simonsick, 1995) and poor sleep quality (Blackwell, Yaffe, Ancoli-Israel, 2011; Martin, Fiorentino, Jouldjian, Josephson, & Alessi, 2010). Sleep disturbances among older adults include difficulty in falling asleep or maintaining asleep, long fragmented sleep [wakefulness after sleep onset> five minutes (Ensrud et al., 2009)], daytime sleepiness, early morning awakening, decreased total sleep time, decreased sleep efficiency [percentage of total sleep time while in the bed (Ensrud et al., 2009)], increased sleep latency [amount of time for falling asleep while in bed (Ensrud et al., 2009)] (Edwards et al., 2010; Espiritu, 2008), and increased number and length of daytime naps (Edwards et al., 2010). Studies have shown that the most common

objective symptoms measured by polysomnography are changes in sleep architecture. These changes include reduction of total sleep time (around 10 minutes per decade), sleep efficiency, stage three and four of non-rapid eye movement (NREM) sleep, which is called slow wave sleep (SWS) (2% decrease of proportion per decade from the age of 60), rapid eye movement (REM) sleep (from the age of 60) (Edwards et al., 2010; Espiritu, 2008), and number of sleep cycles per night (Edwards et al., 2010). Along with these reductions, however, increases among older adults have been found in the following sleep characteristics: sleep latency, stage one and two of NREM sleep, and the number of long fragmented sleep (Edwards et al., 2010; Espiritu, 2008).

These finding are important because sleep, both NREM and REM sleep, plays an important role in the encoding and consolidation of episodic memory (Poe, Walshz, & Bjorness, 2010; Rauchs, Desgranges, Foret, & Eustache, 2005). Sleep deprivation, including partial or total sleep deprivation, (Ellenbogen, Hulbert, Jiang, & Stickgold, 2009; Fenn, Gallo, Margolish, Roediger, & Nusbaum, 2009; Drosopoulos, Windau, Wagner, & Born, 2007; Lahl & Pietrowsky, 2007; Yoo, Hu, Gujar, Jolesz, & Walker, 2007; Hu, Stylos-Allan, & Walker, 2006; Rauchs et al., 2004; Ficca, Lombardo, Rossi, & Salzarulo, 2000) and sleep disorders (e.g., sleep apnea) (Gagnon et al., 2014) were associated with impaired episodic memory. Evidence for the association between episodic memory and sleep comes predominantly from studies of young adults; however, this relationship is not yet well studied in older adults.

Purpose

The purpose of this systematic literature review was to summarize the current findings about the relationship between sleep disturbances and episodic memory in older adults and to comment on whether the relationship evident for older adults parallel those already established for younger persons.

Methods

A systematic literature review was conducted of current studies that investigated the relationship between self-reported or objective sleep disturbances and episodic memory among older adults. The databases searched were PubMed, CINAHL, PsycINFO, Medline, EBM-Reviews Cochrane. The time frame was from past to May 2014. Keywords used included memory, episodic memory, sleep, and sleep disturbances. The inclusion and exclusion criteria for selection of literature are presented in Table 2.1.

Table 2.1

Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
Research goal was to explore the relationship between sleep problems or deprivation and cognitive function including episodic memory	Research goal was only focus on relationship between sleep-related brain wave change or cellular or molecular mechanism and cognition rather than sleep problems
Written in English	Written in non-English
Research subject: human	Research subject: non-human
Age range: sample included at least some participants 65 years and older	Age range: not include participants 65 years and older
Data-based paper including primary and secondary analysis research paper, clinical trial, randomized controlled trial, and meta-analysis	Non-research paper: literature review, systematic literature review, or editor letter
Sample included healthy older adults	

Results

Results of the literature search produced 29 data-based publications that were categorized by study design (Grimes & Schulz, 2002) (See Table 2.2). A summary of study results are

presented in Table 2.3 and comparisons of results are presented in Table 2.4 in supplementary materials.

Table 2.2.

Categories of Current Data-based Publications (n=29)

Type of studies	Number of studies
Descriptive studies	8
Analytical studies	16
Non-randomized controlled experimental studies	3
Randomized controlled experimental studies	2

Group 1: Descriptive Studies

Five of eight descriptive studies investigated the association between self-reported sleep characteristics and episodic memory in older adults. Sutter and colleagues (2012) investigated the relationship between self-reported sleep quality and cognitive functions (i.e., episodic memory, processing speed, verbal fluency, reasoning, executive function, and inhibition), along with subclinical depression, among 96 healthy older adults (mean age: 72 years). Results indicated that sleep quality was significantly and moderately correlated with free recall ($r=-0.23$, $p<.05$) and recognition ($r= -0.23$, $p<.05$) of memory test and subclinical depression ($r=0.41$, $p<.001$) after controlling for age and use of sleep medicine. However, regression results indicated that sleep quality, subclinical depression, and the interaction term of sleep quality and subclinical depression were not significant predictors of episodic memory (Sutter, Zőllig, Allemand, Martin, 2012).

Kronholm and colleagues (2009) conducted a similar study among 6,269 healthy adults aged 30 years and older. Results indicated that word list learning was predicted by self-reported sleep time and fatigue, after controlling socio-demographic factors (i.e., gender, age, and

education) and health factors (R^2 = 0.34, p<.001). Word list delayed recall was predicted by self-reported sleep time, after controlling socio-demographic and health factors (R^2 = 0.12, p=.011). Self-assessment of memory were explained by self-reported fatigue and insomnia, after controlling socio-demographic and health factors (R^2 = 0.30, P<.05). Self-reported sleep characteristics including fatigue, sleep time, and insomnia or sleep disorder were significantly associated with episodic memory in this sample. Self-reported sleep time had a reverse U-shaped association with episodic memory. Individuals with 7-8 hours sleep time had better performance on learning and recall tests than the shorter sleepers (sleep time ≤ 6 hours) (p <.05) and longer sleepers (sleep time ≥ 9 hours) (p<.05). Compared to 7-hour and 8-hour sleepers, the shorter and longer sleepers had a three- to four-fold lower odds ratio for reporting "very good" or " good" in self-assessment of memory, indicating that older individuals with longer or shorter sleep time felt they had poor memory. Fatigue was significantly associated with poorer self-assessment of memory (Kronholm et al., 2009).

Schmutte and colleagues (2007) investigated the relationship between self-reported sleep problems and cognitive functions among 375 non-demented older adults (mean age: 79.6 years). Results indicated that after controlling covariates, sleep latency was significantly correlated with episodic memory (information: r= -0.19, p<.001; vocabulary: r=-0.18, p<.001). Older adults with longer sleep latency, particularly over 30 minutes, had significantly poorer episodic memory performance than the group with shorter sleep onset latency (information: p=.007; vocabulary: p=.001). Older adults with ≤ 4 hour sleep and > 9 hour sleep had significantly poorer episodic memory performance than the group with 5-6 hour and 7-8 hour sleep (information: p=.009, vocabulary: p=.01), supporting a reverse U-shape relationship between self-reported sleep time and episodic memory (Schmutte et al., 2007).

Tworoger and colleagues (2006) explored the association between self-reported sleep problems and episodic memory among 1,852 older women (age: 70-81 years). Compared with women with sleep time of 7 hours, women with sleep time ≤ 5 hours had an increased risk of decreased episodic memory (OR:1.53, 95% CI 0.77-3.06) and had 0.07 standard unit lower in episodic memory. Compared with women who rarely or never had difficulty in falling or staying asleep, women who regularly had difficulty in falling or staying asleep had an increased risk of decreased episodic memory (OR: 1.45, 95% CI: 0.74, 2.85) and women who regularly had difficulty in sleeping scored a mean 0.18 points lower on episodic memory test. Taken together, these results indicated that shorter sleep time and difficulty in falling and staying asleep are associated with decreased episodic memory in older women (Tworoger, Lee, Schernhammer, & Grodstein, 2006).

Gamaldo and colleagues (2008) explored the association between self-reported difficulties in falling asleep and episodic memory among 174 older African American persons (mean age: 72.74 years). Results showed that after controlling age, educational gender, health, income, and depression, problems of falling asleep were not correlated with episodic memory ($p>.05$) nor did they predict it ($p>.05$) (Gamaldo, Allaire, & Whitfield, 2008).

Two of the eight descriptive studies evaluated sleep by objective measurement to investigate the relationship between sleep disturbances and episodic memory in older adults. Mazzoni and colleagues (1999) explored this relationship in 30 healthy older adults (mean age: 68 years). Results of word recall were positively correlated with average length of REM/NREM sleep cycles ($r=0.48$, $p<.01$) and the proportion of time spent in NREM/REM sleep cycle over total sleep time ($r=0.39$, $p<.05$), suggesting that time and proportion of sleep cycles are associated with episodic memory in older adults (Mazzoni et al., 1999).

Oosterman and colleagues (2009) found that among 144 healthy older adults (mean age: 69.5 years), intra-daily variability of sleep-wake rhythm was negatively correlated with performance on a 15-word list learning task ($r=-0.34$, $p<.001$), a pattern recognition memory test ($r=-0.20$, $p<.05$), and summary result of episodic memory tests ($r=-0.31$, $p<.001$). The amplitude of the rhythm was positively correlated to list learning ($r=0.22$, $p<.01$), digit span forward ($r=0.17$, $p<.05$), and summary result of episodic memory ($r=0.20$, $p<.05$). The intra-daily variability was a significant predictor of summary result of episodic memory ($\beta = -0.19$ $p<.01$). A greater fragmented sleep-wake rhythm was associated with poorer episodic memory, while a higher level of activity amplitude was associated with better episodic memory (Oosterman, van Someren, Vogels, van Harten, & Scherder, 2009).

One study has suggested possible relationship between episodic memory and both self-reported and objective sleep reporting. Hart and colleagues (1995) investigated the association between sleep disturbances and episodic memory among 78 older adults with insomnia (mean age: 65 years). Immediate recall of a word list was significantly predicted by total sleep time recorded in a sleep diary ($p<.05$), while results for delayed recall of the word list were explained by total sleep time measured by polysomnograph ($p<.01$) (Hart, Morin, & Best, 1995).

Group 2: Analytical Studies

In addition to descriptive studies, 16 analytical studies were found that investigated the relationship between sleep and episodic memory in older adults by comparing individuals with different sleep characteristics, cognitive levels, or ages, or across more than one time points. Three of these studies explored the relationship between self-reported sleep time and episodic memory. Ferrie and colleagues (2011) recorded self-reported sleep across two time points: baseline (1997-1999) and follow-up (2003-2004) among 5,431 middle- age and older adults (age:

45-69 years). Only males with 7 hours sleep in the follow-up stage had better performance in the recall test than did the groups with $<$ 5 hours, 6 hours, 8 hours, and $\geq$ 9 hours sleep (p=.03). Self-reported sleep time had a reverse U-shaped association with episodic memory. The longer and shorter sleep time were associated with decreased episodic memory, though the authors noted that further investigation would be needed to confirm their results. Decreased sleep time from 7-8 hours to $\leq$ 6 hours and increased sleep time from 7-8 hours to $\geq$ 9 hours overtime were associated with decreased episodic memory but these results were not significant (p>.05) (Ferrie et al., 2011).

Xu and colleagues (2011) examined the relationship between self-reported sleep times and daytime sleepiness, and episodic memory among 28,670 older adults (age: 50-85 years). Their findings demonstrated a reverse U-shaped association between self-reported sleep time and episodic memory with a peak at 7 hours (p-value of trend: 3hours to 7 hours<.001; p-value of trend 7 hours to 10 hours <.001). Compared to individuals with 7-hour sleep time, those with the shortest sleep time (3-4 hours) (p=.007) and longest sleep time ($\geq$ 10 hours) (p<.001) had significantly greater risk of poor episodic memory. Compared to the group without naps or with naps of less than 1 day per week, the group with naps 4-6 days per week (p<.005) and daily (p<.005) had significantly poorer performance on a word-list delayed recall test. Participants who felt tired in the morning at one to two days per week (p= .04) or almost daily (p=.01) had a significantly greater risk of poorer performance on the recall test than did the participants who never felt tired in the morning or only felt tired less than one day per week. The increased rate of morning tiredness was significantly correlated with poorer episodic memory (p-value for trend<.001) (Xu et al., 2011).

Similarly, Loerbroks and colleagues (2010) explored the association between self-reported sleep time and episodic memory among 689 older adults (age: 70 years and older). Self-reported sleep time was recorded in two stages: baseline stage (1992-1995) and follow-up stage (2002-2003). Compared to participants with 7 hours of sleep time, participants with sleep time ≥ 9 hours had a moderately but not significantly increased of risk of declined episodic memory. Individuals whose sleep time increased from 7-8 hours in the baseline stage to ≥ 9 hours in the follow-up stage had approximately a two-fold higher risk of poor episodic memory (prevalence ratios = 1.98, 95% CI: 1.04 -3.78) (Loerbroks, Debling, Amelang, & Stűrmer, 2010).

Additionally, four analytical studies demonstrated that other self-reported sleep characteristics were associated with episodic memory in older adults. Zimmerman, Bigal, Katz, Brickman, and Lipton (2012) explored the relationship between difficulties of sleep onset and maintenance, cognitive functions, and cognitive reserve among 549 older adults (mean age: 79.7 years). The group with difficulties of sleep onset and maintenance did not have significantly poorer episodic memory than did the group without this sleep problem. Cognitive reserve did not appear to influence the relationship between difficulties of sleep onset and maintenance and episodic memory (Zimmerman et al., 2012).

Nebes, Buysse, Halligan, Houck, and Monk (2009) showed that among 157 older adults (age: 65-80 years), compared to participants with good sleep quality (Pittsburgh Sleep Quality Index ≤ 5), those with poor sleep quality (Pittsburgh Sleep Quality Index > 6) did not have significantly poorer performance on immediate (p=.49) and delayed recall (p=.43) (Nebes et al., 2009). This result did not support the posited relationship between sleep disturbances and episodic memory in older adults.

Haimov and colleagues (2006) explored the relationship between insomnia and episodic memory among 73 older adults (mean age: 70.4 years). Evaluation of episodic memory included immediate and delayed recall, learning rate, recognition, proactive interference (capacity to learn a new list of words under the inference of early learned word), retroactive interference (ability to remember learned word list under the inference of new word list), and temporal order judgment of word list. Older adults with insomnia did not recall significantly fewer words than older adults without insomnia in including both immediate and delayed recall score ($p = .09$). There was no significant difference in recognition score between the older adults with and without insomnia ($p = .12$). Older adults without insomnia, however, were better than those with insomnia at resisting effect of proactive interference in word list learning ($p = .047$). Older adults without insomnia had more accurate judgment of the temporal order of word in the learning than older adults with insomnia ($p = .04$) (Haimov, 2006). These results indicate that insomnia is related to poor episodic memory performance in older adults.

Ohayon and his colleagues (2002) investigated the association between daytime sleepiness and cognitions among 1,026 older adults (age: 60 years and older). Individuals with daytime sleepiness demonstrated significantly worse performance in all dimension of measured cognitive functions including episodic memory ($p < .001$). In addition, participants who took unintentional naps had worse episodic memory performance than participants who took intentional naps or never took naps ($p < .05$). Moreover, daytime sleepiness was a predictor of increased risk of difficulties with episodic memory (OR: 2.0, 95% CI, 1.3-3.0, $P < .01$) (Ohayin & Vecchierini, 2002).

Additionally, four studies compared the sleep characteristics and episodic memory function in young and older adults. Wilson and colleagues (2012) explored the effect of sleep on

the episodic memory and motor skill learning among 24 young adults (20 to 34 years old), 32 middle-age adults (35 to 50 years old), and 31 older adults (51 to 70 years old). Among all participants, after normal sleep, the forgetting rate was 2.5% in delayed recall test and after a wakeful break, the forgetting rate was 10.7%. Young participants had higher correctly recalled word pairs in delayed recall test after normal sleep than them after a wakeful break (p=.005). Even though the middle-age and older participants had higher forgetting rates, they still performed better in the delayed recall test after normal sleep (p=.01 for middle-age adults, p=.007 for older adults) than after a wake break. These results suggest that adequate sleep may benefit episodic memory among all age groups (Wilson, Baran, Pace-Schott, Ivry, & Spencer, 2012).

Aly and Moscovitch (2010) examined the influence of sleep on episodic memory among 10 younger adults (age: 19- 29 years) and 12 older adults (age: 69-80 years). The 10 younger adults performed better on the proportion of story recall (i.e., recalled number of story units divided by the encoded number of story units) (p=.001) and memory of personal experience test (p=.001) after normal sleep than after a wakeful break. The 12 older adults performed better on the proportion of recall (p=.014) and the memory of personal experience test (p=.027) after normal sleep than after a wake break. A benefit score for episodic memory was determined by the proportion of recall after sleep minus proportion of recall after waking. Sleep time was positively correlated with the benefit score for episodic memory in the older adults (r= 0.78, p=.008) although study sample was small (Aly & Moscovitch, 2010).

Rauchs and colleagues (2008) compared the association between sleep parameters, sleep-related brain waves, and episodic memory among 14 patients with Alzheimer's disease (mean age: 76.9 years), 14 healthy older adults (mean age: 75.1 years), and 14 younger adults (mean

age: 23.4 years). Healthy older adults had significantly lower scores on the test of delayed free recall of a story than did younger adults ($p<.05$). Polysomnograph results showed that healthy older adults had a significant decrease in the total number, mean intensity, and mean weight intensity of both slow and faster sleep spindle ($p<.001$) than did younger adults. Compared to younger adults, healthy older adults had a decrease in total sleep time ($p<.01$), a decrease in sleep efficiency ($p<.001$), an increase in awakenings ($p<.01$), an increase in wakefulness after sleep onset ($p<.001$), a decrease in SWS ($p<.01$), and a decrease in REM ($p<.01$).These differences were not found in comparison of healthy older adults and patients with Alzheimer's disease. Only the mean intensity of all sleep spindles ($r=0.58$, $p<.03$) and of fast sleep spindle ($r=0.62$, $p<.02$) were significantly correlated with the outcome of the immediate free recall of story in Alzheimer patients. In other words, episodic memory of the Alzheimer patients was significantly associated with the sleep-related brain wave. This relationship was not investigated among the younger and healthy older adults (Rauchs et al., 2008).

Spencer, Gouw, and Ivry (2007) investigated the difference between reaction time during an episodic memory task after sleep and wake interval among 32 older adults (mean age: 59.0 years) and 38 younger adults (mean age of 20.8 years). Reaction time of the learning task was significantly different among younger and older adults after wake and sleep interval ($p<.001$). The interaction of age and learning schedule was significant for the mean reaction time of learning task ($p<.003$). The younger group had a significantly greater reduction for reaction time in the learning task after a sleep interval than the older group had ($p<.001$). However, this association was not seen in the older adults (Spencer et al., 2007).

Sleep parameters and episodic memory have been compared across older adults groups with different levels of cognitive functioning**.** Five studies compared sleep characteristics and

episodic memory in the healthy older adults and patients with Alzheimer's disease or with mild cognitive impairment. Cochrane and colleagues (2012) examined the relationship between circadian rhythms, sleep, ambulatory activity and cognitive functions among 26 community-dwelling older adults (age: 55 years and older). According to the normalized results of National Adults Reading Test which was used to determine general intellectual status, the sample was divided into two groups: intact (n=16, mean age: 71.9 years) and declined (n=10, mean age: 70.9 years). There were no significant differences in all sleep characteristics from actigraphy and sleep diary between intact and declined groups. Only sleep time was significantly correlated with the results of Logical Memory I ($r=-0.54$, $p<.05$) among all subjects (Corhrane, Robertson, & Coogan, 2012). The sample size of this study, however, may affect the overall power.

Westerberg et al. (2012) compared sleep parameters and episodic memory between 16 healthy older adults (mean age: 72.7 years) and 8 patients with amnestic mild cognitive impairment (mean age: 75.6 years). Patients with amnestic mild cognitive impairment had significantly poorer performance than did healthy older adults in recall test of word list ($p<.001$), and fact recognition ($p<.001$). The interaction term of test time (before and after sleep) and groups was significant for word list recall ($p<.05$). Older adults performed better after sleep than before sleep. However, patients with amnestic mild cognitive impairment did not. Patients with amnestic mild cognitive impairment had significantly shorter SWS ($p<.05$), less percentage of SWS ($p<.05$), smaller ratio of SWS minutes verse REM minutes ($p<.05$). Patients with amnestic mild cognitive impairment had significantly reduced delta ($p<.05$) and theta waves ($p<.05$) compared to healthy older adults in NREM sleep. No sleep parameters were significantly associated with test results of episodic memory (Westerberg et al., 2012).

Similarly, Hot and colleagues (2011) compared the sleep characteristics and episodic memory function among 14 healthy older adults (mean age: 76.7 years) and 14 Alzheimer patients (mean age: 76.7 years). Alzheimer patients had significantly lower sleep efficiency than the healthy older adults ($p<.05$). Faster theta rhythm during sleep was positively correlated with the result of delayed cue recall test ($r=0.64$, $p<.05$) and negatively correlated with the forgetting rate ($r=-0.64$, $p<.05$) among Alzheimer patients. However, these relationships were not found in healthy older adults (Hot et al., 2011).

Another similar study was conducted by Westerberg et al. (2010) which investigated the association between sleep characteristics and episodic memory among 10 healthy older adults (mean age: 72.5 years) and 10 patients with amnestic mild cognitive impairment (mean age: 71.1 years). Among patients with amnestic mild cognitive impairment, results from a 24-hour recognition memory task were related to time in bed ($r=0.20$, $p<.05$), sleep fragmentation index ($r=0.31$, $p<.05$) from actigraph, wake time ($r=0.23$, $p<.05$), self-reported sleep assessment ($r=0.29$, $p<.05$), self-reported sleep efficiency ($r=0.44$, $p<.05$), and self-reported sleep difficulty ($r=-0.13$, $p<.05$) from the Karolinska Sleep Diary. However, significant correlations were not evident for the control group. Among overall participants, variability of time in bed ($r=-0.48$, $p<.05$), total sleep time ($r=-0.53$, $p<.05$), sleep latency ($r=-0.49$, $p<.05$), and sleep fragmentation ($r=-0.50$, $p<.05$) from actigraphy were significantly correlated with a paragraph learning task (Westerberg et al., 2010).

Bonanni and colleagues (2005) explored the association between sleep parameters and episodic memory among 11 drug-free patients with mild Alzheimer's disease (mean age: 65.6 years) and 9 moderate Alzheimer's disease (mean age: 64 years) and 12 healthy older adults (mean age: 61.1 years). Compared to patients with mild Alzheimer's disease and healthy older

adults, scores on the multiple sleep latency test were significantly lower in patients with moderate Alzheimer's disease ($p<.05$), indicating that these patients had the highest degree of daytime sleepiness. Patients with mild Alzheimer's disease had a significantly reduced score in the multiple sleep latency test than did the healthy older adults ($p<.05$), suggesting that these patients had a higher degree of daytime sleepiness. Among all patients with Alzheimer's disease, result of multiple sleep latency test was significantly correlated with verbal digit span ($r=0.56$, $p<.05$) and story recall ($r=0.67$, $p<.05$), suggesting that patients with higher degree of daytime sleepiness had poorer episodic memory (Bonanni et al., 2005).

Group 3: Non-Randomized Controlled Experimental Studies

The effect of artificial sleep manipulation on the episodic memory among older adults was explored in three non-randomized control trials. Van Der Werf, Altena, Vis, Koene, and van Someren (2011) explored the effects of disruption of SWS and reduction of slow wave activity on episodic memory among 13 older adults (mean age: 60.1 years). Participants had significantly lower scores on the true positive response on a word list task after a night with a reduction in slow wave activity by SWS disruption than after a night with normal sleep ($p=.008$). After disrupted SWS, participants had significantly smaller difference between true positive rate and false positive rate than after normal sleep ($p<.007$). Another effect of SWS disruption and reduced slow wave activity was a significant reduction in the right hippocampal activity compared to normal sleep. This study suggested that disrupted SWS and reduction in slow wave activity are associated with reduced accuracy of episodic memory (Van Der Werf et al., 2011).

Stenuit and colleagues (2008) explored the influence of sleep restriction on episodic memory among 10 healthy younger females (mean age: 23.2 years) and 10 older females (mean age: 60 years). All participants followed a sleep-wake schedule: one baseline night (23pm -7am,

8hrs), 3 continuous sleep nights (1am-5am, 4hrs), one recovery night (11pm -7pm, 8hrs). The free recall rate of the immediate and delayed recall during sleep restriction was significantly lower than in normal sleep for both age groups ($p<.01$), suggesting that sleep restriction may impair episodic memory in daytime (Stenuit & Kerkhofs, 2008).

Fenn and colleagues (2009) investigated the effect of normal sleep on the episodic memory among 92 healthy adults. All participants were equally assigned to one of two groups: one with sleep and the other without sleep. Compared to the group without sleep, the group with sleep had a lower rate of false recognition ($p<.05$) and better episodic memory accuracy ($p<.01$) (Fenn et al., 2009).

Group 4: Randomized Controlled Experimental Study

In addition to non-randomized control trials, two randomized control trials investigated the influence of different stages of sleep on episodic memory among older adults. Backhaus and colleagues (2007) explored the influence of early and late sleep schedule on the performance of declarative memory tasks, which include episodic memory, in 16 healthy younger adults (mean age: 20.4 years) and 14 middle-aged adults (mean age: 50 years). All participants in each age group were randomly assigned into one of two experimental groups: early and late sleep schedule. Outcomes demonstrated that younger group retained significantly more learned word pairs than middle-aged group did after early sleep schedule ($p<.001$) and late sleep schedule ($p=.02$). Only SWS was a significant predictor of retention of the word pairs ($\beta =0.51$, $p=0.004$) in all participants. Retention of the word-pair was generally worse in the late sleep schedule compared to those with the early sleep schedule ($p=0.005$). The retention of the word-pair was significantly correlated with the percentage of SWS during early sleep ($r=0.51$, $p=.004$).

Outcome of this study suggests that declarative memory is associated with sleep, particularly SWS in healthy adults (Backhaus et al., 2007).

To explore the effect of sleep schedule on episodic memory, Hornung Regen, Danker-Hopfe, Schredl, and Heuser (2007) investigated the effect of REM sleep deprivation and stage 2 NREM sleep deprivation on episodic memory among 107 healthy older adults (mean age: 66.1 years). All participants were randomly assigned to one of five groups: selective REM sleep deprivation; stage 2 NREM sleep awakening; REM rebound; REM augmentation by acetylcholinesterase Inhibitor; and a control group. The number of errors in the episodic memory task was significantly lower after sleep than before sleep in all experimental groups. However, the improvement in performance after sleep did not significantly correlate with any sleep parameters. No differences among these five groups were found in results of the episodic memory task (Hornung et al., 2007). These findings indicate that episodic memory may be improved after normal or disturbed sleep, but the relationship between sleep and episodic memory requires further investigation.

Discussion

This systematic literature review summarized the relationship between sleep disturbances and episodic memory among older adults from 29 publications. Among these 29 publications, 6 of them clearly indicated a reversed U-shape relationship between self-reported sleep time and episodic memory (Ferrie et al., 2011; Loerbroks et al., 2010; Kronholm et al., 2009; Oosterman et al., 2009; Schmutte et al., 2007; Tworoger et al., 2006). They all indicated that older adults with 7-8 hour sleep time had better episodic memory than older adults with $\leq$ 6 hours sleep or $\geq$ 9 hours sleep (Ferrie et al., 2011; Loerbroks et al., 2010; Kronholm et al., 2009; Oosterman et al., 2009; Schmutte et al., 2007; Tworoger et al., 2006). These results suggest that too short or too

long sleep time are related to decline of episodic memory. However, the measure of sleep time was only from self-reported and no objectively measured outcomes were studied. Objectively measured sleep time demonstrated a linear correlation with episodic memory. This phenomenon may reflect the influence of depressive symptoms on self-reported sleep time. Bliwise and colleagues (1993) found that older adults with more depressive symptoms tended to under- or overestimated sleep time (Bliwise, Friedman, & Yesavage, 1993). Depressive symptoms were significantly correlated with decreased episodic memory in older adults (Fotuhi, Do, & Jack, 2012; Beaudreau & O'Hara, 2009; Panza et al., 2009; Gonzalez, Bowen, & Fisher, 2008). Thus, future studies will need to explore the role of depressive symptoms in this reverse U-shape relationship.

Longitudinal changes in sleep time have been studied. The studies by Ferrie et al. (2011) and Loerbroks et al. (2010) indicated that decreased sleep time from 7-8 hours to $\leq$ 6 hours and increased sleep time from 7-8 hours to $\geq$ 9 hours over two and five years was associated with decreased episodic memory (Ferrie et al., 2011) or increased prevalence of poor episodic memory (Loerbroks et al., 2010) but further research is needed to confirm this association. These two longitudinal studies, however, only looked at the relationship between longitudinal changes of sleep time and episodic memory at a single time point rather than changes of sleep time related to the possible natural decline or change of episodic memory over time with aging. In a longitudinal study regarding self-reported time of sleep, Lo, Loh, Zheng, Sim, & Chee (2014) found that each hour of self-reported sleep reduction across 2 years was significantly related to an annual decline of 0.67% in global cognitive function ($p=.05$) among healthy older adults (Lo et al., 2014). However, this study did not find a similar relationship with sleep reduction in

episodic memory domain. Again, these researchers only used self-report and not objectively measured indicators of sleep time.

In addition to sleep time, other self-reported sleep disturbances have been found to be associated with poorer episodic memory in older adults: difficulty in falling asleep and maintaining sleep (Sutter etal., 2012; Zimmerman et al., 2012; Westerberg et al., 2010; Kronholm et al., 2009; Gamaldo et al., 2008; Schmutte et al., 2007; Tworoger et al., 2006), daytime tiredness and fatigues (Xu et al., 2011; Kronholm et al., 2009; Ohayon & Vecchierini, 2002), insomnia or sleep disorder (Haimov, 2006), longer sleep latency, higher level of sleep fragmentation (Westerberg et al., 2010; Schmutte et al., 2007; Tworoger et al., 2006), and daytime sleepiness (Xu et al., 2011; Kronholm et al., 2009; Bonanni et al., 2005; Ohayon & Vecchierini, 2002). However, it is still unclear which of these parameters are most importantly associated with episodic memory. If this were known, it would suggest direct ways to influence sleep changes leading to improving deceased episodic memory.

In addition to self-reported sleep problems, objectively measured sleep parameters (i.e, actigraphy and polysomnography) were significantly associated with episodic memory, specifically: total sleep time (Cochrane et al., 2012; Westerberg et al., 2010; Hart et al., 1995), sleep fragmentation (Westerberg et al., 2010), the time and percentage of SWS (Westerberg et al., 2012), average duration of NREM/REM cycle (Mazzoni et al., 1999), proportion of the time spent on NREM/REM sleep over total sleep time (Mazzoni et al., 1999), and sleep-wake rhythm (Oosterman et al., 2009). However, the results of these studies do not allow determination of which objectively measured sleep characteristics have the strongest relationship to episodic memory.

In addition to observed sleep characteristics, artificial restriction or manipulation of sleep (e.g. deprivation or disruption of SWS) was associated with episodic memory (Van Der Werf et al., 2011; Fenn et al., 2009; Stenuit & Kerkhofs, 2008; Backhaus et al., 2007). Older adults experiencing artificial sleep disruptions performed more poorly on episodic memory tests, particularly following SWS disruption. Sleep, particularly slow wave sleep, appears important for effective episodic memory in older adults (Backhaus et al., 2007). Older adults after normal sleep had better performance in episodic memory tasks. Sleep benefits the episodic memory in this population (Westerberg et al., 2012; Wilson et al., 2012; Aly & Moscovitch, 2010; Hornung et al., 2007).

Among these 29 publications, 14 studies only used self-reported questionnaires to determine sleep disturbances; 9 studies only used objective measurements including polysomngraphy and wrist-worn actigraph device to assess sleep parameter; 4 studies used both self-reported sleep questionnaire and objectively measurement to evaluate sleep; and the remaining 2 studies adapted manipulated sleep schedule to determine the effect of sleep on episodic memory. One of the problems in the field is that there are many approaches to measure sleep, but few studies have looked at multiple approaches simultaneously. It is hard to know which measures will contribute the most to understanding sleep disturbances and episodic memory.

Among the only 4 studies which obtained both self-reported and objectively measured sleep data, only Hart et al. (1995) and Westerberg et al. (2010) correlated the these two domains of sleep parameters to allow a more direct comparison. Sleep efficiency and fragmented sleep from sleep diaries and polysomnographs were significantly correlated ($p<.05$) (Hart et al., 1995) and wake time, bed time and sleep time from sleep diary and actigraphy were significantly

correlated ($p<.05$) (Westerberg et al., 2010). There have been no other studies that have investigated the association between subjective and objective sleep disturbances, so there are no clear indications as to whether self-report or objectively measured sleep parameters better correlated with episodic memory. Thus, it is hard to make a conclusion for future studies to determine either self-reported or objectively measured sleep data should be utilized or both of them are necessary. In addition, it is difficult to compare the relationship between self-reported and objectively measured sleep parameters to episodic memory, which may demonstrate different relationships (i.e., reverse U-shape association in self-reported sleep time and episodic memory and linear relationship between objective sleep time and episodic memory)

Some studies have tried to better understand relationship of sleep and episodic memory through comparing different groups by either age or cognitive status. Among the 16 analytic studies, four of them compared the relationship between sleep parameters and episodic memory among younger and older adults. Results showed that the correlation between sleep disturbances and poorer episodic memory were stronger in younger adults than in older adults (Aly & Moscovitch, 2010), suggesting that the sleep-dependent memory consolidation may be reduced with aging. However, the moderating effect of age in the relationship between sleep and episodic memory needs further confirmation.

Five studies compared the sleep characteristics and episodic memory among healthy older adults to patients with impaired cognitive function. The study by Cochrane et al. (2012) showed that only sleep time significantly correlated with episodic memory. However this result was in the overall sample and not in either group, alone (Cochrane et al., 2012). Westerberg et al. (2012) indicated that healthy older adult obtained sleep benefit for episodic memory, but patients with amnestic mild cognitive impairment did not (Westerberg et al., 2012). Hot et al. (2011)

found these correlations presented in patients with Alzheimer's disease (Hot et al., 2011). Westerberg et al. (2010) found greater sleep disturbances (i.e., bed time, sleep fragmentation, sleep efficiency, and sleep difficulty) were related to poorer episodic memory but only among patients with amnestic mild cognitive impairment and not controls. When correlations were observed in the overall sample, increased sleep disturbances (i.e., bed time, sleep time, sleep latency, and sleep fragmentation) were significantly correlated with poorer episodic memory (Westerberg et al., 2010). Bonanni et al. (2005) found that a higher level of daytime sleepiness was correlated with poorer episodic memory only in patients with Alzheimer's disease and not in healthy older adults (Bonanni et al., 2005). To summarize across these studies, it appears that the relationship between sleep disturbances and episodic memory is stronger among patients with impaired cognitive function than in healthy older adults. Of these studies discussed above, only Westerberg et al.. (2012), Westerberg et al. (2011), and Bonanni et al. (2005) obtained results from individual groups and not just combined groups, making interpretations difficult. As in many of these studies, the total size of these five studies was relatively small (N=20 to 32).

Although there are concerns with studies that have sought to compare results across diagnostic groups, the finding are of particular interest. For example, Spira et al. (2013) have reported that shorter sleep time and poor sleep quality were both associated with greater β-amyloid deposition, a hallmark of Alzheimer pathological change, in the brain in community-dwelling older adults (N=70, mean age: 76 years) (Spira et al, 2013). Although these findings were purportedly healthy adults, the sample did include some non-demented persons with impaired cognition, possibly increasing the opportunity for a significant interrelationship.

This systematic review of the literature does suggest directions for future research. First, future studies should utilize both self-reported and objective methodology to measure sleep.

Second, longitudinal designs to measure sleep and episodic memory are better determine how changes in sleep patterns with aging relate to age- and disease-associated changes in episodic memory. Third, nine studies had just 30 or fewer participants. Thus, sufficient sample size is necessary for future studies. Finally, there is no clear, testable theory has been proposed that links sleep disturbances and episodic memory together, and integrates possible related factors into this relationship conceptually. Thus, building a theory to support the relationship between sleep and episodic memory and integrating possible related factors will be critical for more clinically meaningful and successful interventions.

Table 2.3

The Relationship between Sleep and Episodic Memory in Older Adults

Author	Years	Sample	Design	Measure	Results
			Descriptive		
Sutter et al.	2012	Healthy older adults (N=96, mean age: 72 ± 5.7)	Cross-sectional	Sleep quality: PSQI; Episodic memory: German version of Verbal Learning and Memory Test; Subclinical depression: short version of Geriatric Depression Scale.	The correlation results indicated that sleep quality was significantly correlated with free recall ($r=-0.23$, $p<.05$) and recognition ($r= -0.23$, $p<.05$) of memory tests and subclinical depression ($r=0.41$, $p<.001$). The regression results were significant [$F(5, 95)= 4.39$, $p<.001$, $R^2= 0.20$]. However, sleep quality, subclinical depression, and the interaction term of sleep quality and subclinical depression were not significant predictors of episodic memory after controlling age and use of sleep medications.

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
Kronholm et al.	2009	Healthy adults (N=6,269, age: 30+)	Cross-sectional	Sleep: self-reported habitual sleep time; self-reported insomnia, tiredness, probable sleep apnea, usage of hypnotics; Episodic memory: mean of three trials of the	The results of the learning effect of the word list were explained by fatigue and sleep time (R^2=0.34, p<.001) after controlling sociodemographic factors and health factors. The results of recall rate of the word list were explained by sleep time (R^2= 0.12, p=.011) after controlling sociodemographic factors and health factors. The result of self-assessment of memory was explained by fatigue, exceptional tiredness, and insomnia or sleep disorders (R^2= 0.30, p<.05) after controlling sociodemographic factors and health factors. The individuals with 7-hour

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				learning effect of a list of 10 word, delayed recall test, and self-assessment of memory	in the learning effect of the word list and recall rate of the word list than did the shorter sleepers (sleep time ≤ 6 hours) ($p < .05$) and longer sleepers (sleep time ≥ 9 hours) ($p < .05$). Among longer sleepers, sleep time was negatively correlated with learning effect ($r = -0.21$) ($p < .05$) and recall rate of the word list ($r = -0.21$) ($p < .05$). Among short sleepers, sleep time was positively correlated with the learning effect of word list ($r = 0.16$) ($p < .05$) and recall rate of the word list ($r = 0.10$) ($p < .05$). Compared to 7-hour and 8-hour sleepers, the participants with shorter or

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					longer sleep time had a three- to four-fold lower odds ratio of reporting “very good” or “good” in self-assessment of memory. Fatigue and tiredness were associated consistently and linearly with decreased rate of reporting “very good” or “good” in self-assessment of memory. Probable sleep apnea was independently associated with learning effect and subjective memory assessment; sleep time was independently associated with learning effect; insomnia or sleep disorder was associated with subjective memory assessment.

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
Schmutte et al.	2007	Healthy older adults (N= 375, mean age: 79.6 $\pm$ 3.2, men/women: 134/241)	Cross-sectional	Sleep: 54-item sleep questionnaire; Episodic memory: verbal subset of Wechsler Adult Intelligence Scale (i.e., information and vocabulary sections)	Self-reported sleep onset latency was significantly correlated with the result of information section (r=-0.19, p<.001) and vocabulary section (r=-0.18, p<.001). Compared with the older adults with less than 30 minutes sleep onset latency, those with over 30 minutes sleep latency had significantly poor performance in information section [F(27, 630)= 4.12, p=.007] and vocabulary section [F(27, 630)= 5.41, p=.001]. Compared with the older adults with 5-6 hours sleep and 7-8 hours sleep, those with $\leq$ 4 hours sleep and > 9 hours sleep had

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					significantly poor results of information section [F(3, 265)= 3.92, p=.009] and vocabulary section [F(3, 265)= 3.68, p=.01].
Tworoger et al.	2006	Older women (N=1,852, age: 70-81)	Retrospective, cross-sectional	Sleep: self-reported sleep time within 24 hours, self-reported snoring status, difficulty in falling and staying asleep; Episodic memory: immediate and	Compared with the women with sleep time of 7 hours, women with sleep time ≤ 5 hours had an increased risk of decreased episodic memory (z-score of combined results of the immediate and delayed recall of the East Boston Memory test and10-word list) (OR:1.53; 95% CI 0.77-3.06) and had 0.07 (95% CI: -0.22, 0.08) standard unit lower in episodic memory performance. Compared with women who rarely or never had

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				delayed recall of the East Boston Memory test, delayed recall of the10-word list of Telephone Interview for Cognitive Status	difficulty in falling or staying asleep, women who reported that they regularly had difficulty in falling or staying asleep had an increased risk of decreased episodic memory (OR: 1.45, 95% CI: 0.74, 2.85) and women reporting regularly having difficulty in sleeping scored a mean 0.18 points lower on episodic memory test (95% CI: -0.31, -0.05).
Gamaldo et al.	2008	African Americans (N= 174, mean age: 72.74 ± 5.60, men/ women: 51/ 123)	Cross-sectional	Problems falling asleep: self-reported sleep difficulty in; Episodic memory:	Problems of falling asleep did not correlated with the episodic memory (r=-0.03, p>.05) and did not predict the results of episodic memory ($\beta = -0.07, p > .05$) after controlling age, educational gender, health,

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				California Verbal Learning Test- first trial of list A	income, and depression (not reported F-value and R square)
Mazzoni et al.	1999	Healthy older adults (N= 30, mean age: 68 ± 5, men/women: 17/13)	Cross-sectional	Sleep: PSG; Episodic memory: cue recall of verbal memory test for a list of 20-pair of unrelated words	The average duration of NREM/REM cycle was significantly correlated to the results of word recall in the morning (r=0.48, p<.01). The proportion of time spent in NREM/REM sleep cycle divided by total sleep time was significantly correlated to the results of word recall in the morning (r=0.39, p<.05).
Oosterman et al.	2009	Older adults (N= 144, mean age: 69.5 ± 8.5, men/ women: 90/ 54)	Longitudinal	Sleep-wake rhythm: 7 days continuous	The intra-daily variability for sleep-wake rhythm was significantly correlated with the outcomes of 15-word test (r = -0.34, p<.001),

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				actigraphy [The intra-daily variability for sleep-wake rhythm assessed the fragmentation of sleep-wake rhythm. The amplitude of the sleep-wake rhythm = the average activity during the most	pattern recognition memory (r =-0.20, p<.05) and summary result of episodic memory (r=-0.31, p<.001). The results of the amplitude of the sleep-wake rhythm were significantly correlated with the outcomes of 15-word list test (r =0.22, p<.01), digit span forward (r=0.17, p<.05), summary result of episodic memory (r=0.20, p<.05). The intra-daily variability for sleep-wake rhythm significantly predicted the summary result of episodic memory (β = -0.19 p<.01). The R^2 value was not reported in this study.

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				active 10-hour period (M10) minus the average activity during the least active 5-hour period(L5)] Episodic memory: 15-word test, digital forward, pattern recognition memory, and a summary result of	

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				episodic memory derived from the above three tests.	
Hart et al.	1995	Older adults with primary insomnia (N= 78, mean age: 65 ± 6.9, range: 55-84, men/ women: 28/50)	Longitudinal	Sleep: PSG and sleep diary for two weeks; Episodic memory: Free recall of clustered and unclustered word list	The results of immediate recall of word-lists were explained by the total sleep time in sleep diary (R^2 = 0.06, F=4.8, p<.05) and the results of the percent retained recall of word-lists were explained by the total sleep time in PSG (R^2 = 0.13, F=10.8, p<.01). The wakefulness after sleep onset (r=0.33, p<.01) and sleep efficiency (r=0.23, p<.05) from sleep diary and PSG were significantly correlated with each other.

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
			Analytical		
Ferrie et al.	2011	Healthy older adults (N= 5,431, age range: 45-69 at baseline, men/women: 3,972/1,459)	Prospective cohort, longitudinal	Sleep: self-reported sleep time in 2 stages: baseline (1997-1999) and follow-up (2003-2004); Episodic memory: a 20–word free recall test	The men with sleep time of 7 hours at follow up stage had the highest scores in episodic memory tests, followed by the group with sleep time of 6 hours, the group with sleep time of 8 hours, the group with sleep time of ≤ 5hours, and finally the lowest group with sleep time of ≥ 9 hours (p =.03). Compared to the participants with no change in sleep time, the participants with an increased sleep time from 7 or 8 hours at the baseline to 8 or ≥ 9 hours at the follow-up stage had poorer but not significant performance in the free-recall

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					test (p>.05). Compared to the participants with no change in sleep time, the participants with an a decreased sleep time from 6, 7, or 8 hours at the baseline stage to 6, 7, or ≤ 5 hours at the follow-up stage had poorer but not significant performance in the free-recall test (p>.05).
Xu et al.,	2011	Healthy older Chinese adults (N= 28,670, age range: 50-85, men/women: 7,894/ 20,776)	Cross-sectional	Sleep: self-reported sleep statements; Episodic memory: Delayed word recall test for 10	Compared with other groups, the older adults with 7-hour sleep had best episodic memory (p-value of trend: 3hours to 7 hours <.001; p-value of trend 7 hours to 10 hours <.001). Compared to the group with sleep time of 7 hours, the groups with shortest

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				words	sleep time (3-4 hours) (OR:1.29, CI: 1.07-1.56, p= .007) and longest sleep time (≥ 10 hours) (OR: 1.52, CI: 1.25-1.86, p<.001) had significant risk of poorer episodic memory performance. The increase in the frequency of daytime nap was significantly associated with a decline in episodic memory (p-value for trend =.005). Compared to the group who never had daytime nap or had daytime nap less than 1 day per week, the group who had daytime nap 4-6 days/week (p<.005) and daily (p<.005) had significant lower scores on episodic memory test. Compared to the group

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					who never felt tired or felt tired in the morning less than 1day/week, the group who felt tired in the morning 1-2 days/ week (OR: 1.18, CI: 1.01-1.39, p=.04) or almost daily (OR: 1.27, CI: 1.05-1.53, P=.01) had significant risk of poorer performance in episodic memory test. The increase in morning tiredness was significantly associated with decrease in episodic memory (p-value for trend<.001). The group felt tiredness daily had poorer episodic memory than the group who never or less than 1-2 days/week felt tiredness in the morning (p<.001).

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
Loerbroks et al.	2010	Healthy older adults (N= 689, age: 70+, men/women: 342/347)	Prospective cohort, longitudinal	Sleep: self-reported sleep time at baseline (1992-1995) and follow-up (2002-2003); Episodic memory: delayed recall of 10-word list and the East Boston memory test (including immediate recall and delayed	Compared to the group with sleep time of 7 hours, the group with sleep time ≥ 9 hours had a moderately but not significantly, increased prevalence of impairment of episodic memory (PR=1.71, 95% CI: 0.98- 2.97). The group with increased sleep time (7 or 8 hours to ≥ 9 hours) had two-fold higher prevalence of decreased episodic memory (PR= 1.98, 95% CI: 1.04 -3.78).

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				recall), episodic memory: combine the result of above two memory test	
Zimmerman et al.	2012	Healthy older adults (N=549, mean age: 79.7 $\pm$ 5.0, men/women: 208/341)	Cross-sectional	Sleep: Medical Outcomes Study Sleep Scale; Episodic memory: Free and Cued Selective Reminding Test; cognitive reserve	The group with difficulties of sleep onset and maintenance did not show poorer performance in episodic memory test than did the group without difficulties of sleep onset and maintenance [F(1, 536) = 2.26, p=.13]. The group with >12 educational years did not performed better in episodic memory test than did the group with $\leq$ 12 educational years

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				function: educational years	[F(1, 536) = 0.69, p=.41]. The interaction of educational years and difficulties of sleep onset and maintenance did not have significant effect on episodic memory [F(1, 535) = 1.36, P=.24].
Nebes et al.	2009	Healthy older adults (N= 157, age range: 65-80) divided into good sleepers (n=108) and poor sleeper (n= 49) by the result of PSQI ≤ 5 and > 6, respectively	Cross-sectional	Sleep quality: PSQI; Episodic memory: Logical Memory test of the WMS-revised	The good sleepers performed better on the test for episodic memory than poor sleepers [for logical memory immediate recall (mean± SD): 9.91 ± 2.8 vs 9.56 ± 3.07, t(154) = 0.69, p=.49; for logical memory delayed recall (mean± SD): 10.19 ± 2.84 vs. 9.79 ± 2.92, t(154) = 0.79, p=.43]; however, this difference did not reach statistical significance.

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
Haimov	2006	Older adults (N=73, mean age: 70.4 ± 5.8, men/ women: 45/28)	Cross-sectional	Sleep: Mini Sleep Questionnaire and the Technion Sleep Questionnaire; Episodic memory: the Rey Auditory Verbal Learning test (immediate and delayed recall, learning rate, recognition, proactive	Older adults without insomnia recalled more words than the older adult with insomnia [t(71) =1.31, p=0.09] but not significant. There was no significant difference in the results of recognition test between the older adults with and without insomnia [t(71) = 1.16, p =.12]. The proactive interference × sleep group interaction (trail 1 score – trail 6 score) was significant, [F(1, 66) =2.89, p=0.047], suggesting that resistance to proactive interference among older adults without insomnia was stronger than among older adults with insomnia. The absolute

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				interference test, retroactive interference test, and temporal order judgment of word list)	deviation score reached significance [t(43) =1. 79, p=0.04], suggesting that the temporal order judgment of older adults without insomnia may be more accurate than those with insomnia.
Ohayon et al.	2002	Healthy older adults (n=1026, 28.7%: aged 60-64; 25.4%:aged 65-69; 21.2%: aged 70-74; 24.7% 75+, men/women: 412/614)	Cross-sectional	Sleep (including daytime sleepiness): sleep-EVAL system; Cognitive functions: Cognitive	The participants with daytime sleepiness had a significantly poorer scores on all dimensions of Cognitive Difficulties Scale than the participants without daytime sleepiness (1.75± 2.64 vs. 0.62± 1.29, p<>001). Compared with the participants who took intentional naps and never took naps, the

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				Difficulties Scale	participants who took unintentional naps had higher scores of difficulty in delayed recall (1.63 ± 2.05 in unintentional nap, 0.73 ± 1.58 in never nap, 0.74 ± 1.46 in intentional nap group, p<.05). The predictors of difficulties in delayed recall included daytime sleepiness (OR: 2.0, 95% CI, 1.3-3.0, P<.01), male (OR: 1.5, 95% CI, 1.3-1.7, P<.01), depressive mood (OR: 1.6, 95% CI, 1.1-2.4, P<.05), and anxiety (OR: 1.5, 95% CI, 1.0-2.3, p<.05).

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
Wilson et al.	2012	Healthy young adults (n=24, age: 20-34, men/women: 14/10), middle-age adults (n=32, age: 35-50, men/women: 18/14), and older adults (n=31, age: 51-70, men/women:18/13)	Cross-sectional	Sleep time: self-reported sleep time and PSQI; Sleep effect on episodic memory; different sleep learning schedule (AM-PM-AM vs. PM-AM-PM); Episodic memory: a Word pair learning task	The forgetting rates after sleep interval was 2.5% while the forgetting rates after wake interval was 10.7% among overall sample. The of episodic memory performance was better after sleep interval than after wake interval among young adults [$t(22) = 3.1$, $p=.005$], middle-age adults [$t(28) = -2.7$, $p=0.01$], and older adults [$t(24)= -2.9$, $p=.007$]. However, age and sleep time were not significant predictors of sleep benefit scores [$F(2, 74)= 0.28$, $p=.76$].

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				Including immediate and delayed recall test, forgetting rate of each recall test. Sleep benefit scores = difference of immediate and delayed recall results after sleep – difference of immediate and	

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				delayed recall results after wake interval	
Aly and Moscovitch	2010	Healthy younger adults (n=10, age: 19-29); older adults (n= 12, age: 69-80) following normal wake or normal sleep	Cross-sectional	Sleep: St. Mary's Hospital Sleep Questionnaire and PSQI; Episodic memory: Logical Memory Subscale of the WMS-Ⅲ and 12 questions about previous experience	In younger adults, the proportional recall (number of story units recalled at test/ number of story units recalled at encoding) and memory for personal experience were greater after sleep than after a wake break [t(9) = 4.54, p=.001 for proportional recall; t(9) = 5.87, p=.001 for personal experience]. In older adults, the proportional recall and the memory for personal experience were greater after sleep than after a wake break

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					[t(9) = 3.06, p=.014 for proportional recall; t (9) = 2.64, p=.027 for the memory for personal experience]. The total sleep time in the older adults was significantly correlated with the episodic memory benefit scores from sleep (WMS proportion recall after sleep – WMS proportion recall after waking) (r=0.78, p=.008).
Rauchs et al.	2008	AD patients (n=14, mean age: 76.9 ± 4.1; men/women: 5/9), healthy older adults (n=14, mean age: 75.1	Cross-sectional	Sleep: PSG for one night; Episodic memory: the Grober and Buschke's task	Healthy older adults had poorer performance on delayed free recall of story recall task (7.1 ± 1.7 vs. 8.6 ± 1.9, p<.05) than young adults. Compared to young adults, healthy older adults had a significant decrease

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
		± 4.6; men/women: 5/9), and healthy younger adults (n= 14, mean age: 23.4 ± 3.1; men/women: 7/7)		and a 12-item story recall task taken from the Batterie d'efficience mnesique 144 memory battery	in total sleep time (387.3± 65.7 vs. 452.2± 41.7, p<.01), a decrease in sleep efficiency (78.5± 11vs. 90.9±3.7, p<.001), an increase in awakenings (22.4 ± 12 vs. 10.4 ± 5.2, p<.01), an increase in wakefulness after sleep onset (85.8 ±42.9 vs. 26.1 ± 10.5, p<.001), an increase in stage 1 of NREM sleep (12.4 ± 5.2 vs. 6.6± 2.7, p<.001), an increase in stage 2 NREM sleep (61.2 ±4.4 vs. 52±7.2, p<.001), a decrease in SWS (14.1 ±6.6 vs. 23.1±8.1, p<.01), and a decrease in REM sleep (12.3 ± 5.5 vs. 18.3 ± 4, p<.01).

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					These differences did not show between healthy older adults and AD patients. Compared to young adults, older adults had a decrease in total number [F (1, 25) =19.4, p<.001], mean intensity [F(1,25)=44.4, p<.001], and mean weight intensity [F(1,25)=21.5, p<.001] of both slow and fast sleep spindles. These differences did not show between healthy older adults and AD patients. The mean intensity of all (r=0.58, p<.03) and of fast sleep spindles (r=0.62, p<.02) in AD patients were significantly correlated to immediate free recall of story recall task.

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
Spencer et al.	2007	Health older adults (n= 32, mean age: 59.0 ± 11.1; men/ women: 17/15) and healthy young adults (n= 38, mean age: 20.8 ± 2.1; men/women: 17/21)	Cross-sectional	Explicit (declarative) memory: explicit sequence learning task	The results of reaction time were different in different age groups in different sessions. The effect of age was significant for the mean reaction time of explicit tasks [F(1, 90) = 31.1, p<.001]. Effect of the age× session interaction [F (2, 90) = 6.0, p<.003] was significant for mean reaction time of explicit task. Compared to the older group, the younger group showed significantly greater reduction of reaction time of explicit task after 12-hour break with sleep on explicit task [F(1, 28) = 33.2, p<.001].

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
Cochrane et al.	2012	Community-dwelling older adults (intact cognition: n=16, mean age: 71.94± 2.53, men/women: 5/11; declined cognition: n=10, mean age: 70.90 ± 1.5, men/women: 6/4)	Longitudinal	Sleep: wrist actigraphy for 7 days and sleep diary; Episodic memory: subtests of WMS: Logical Memory I and II, Verbal Paired Associates I and II, and Visual Reproduction I and II	The intact group had significant better performance than did the decline group in the tests of Logical memory I (11.5 ± 0.53 vs. 8.3± 0.83, p=.002), Logical Memory II (11.5 ± 0.58 vs. 8.7 ± 0.78, p=.008), and Visual Reproduction II (12.93 ± 0.78 vs. 10.77± 0.64, p=.008). There were no significant difference among all sleep parameters (i.e., sleep duration, bed time, wake time, sleep efficiency, wake-up after sleep onset, and sleep latency) between these two groups. Only sleep duration was significantly correlated

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					with the result of Logical Memory I (r=-0.54, p<.05) among overall sample.
Westerberg et al.	2012	Healthy older adults (n= 16 mean age: 72.7 ± 5.1, men/women: 3/13), aMCI patients (n= 8, mean age: 75.6 ± 7.2, men/women: 1/7)	Cross-sectional	Sleep: PSG for 2 nights; Episodic memory: Word-pair recall of 44 related word pairs, Fact recognition, and object priming before and after sleep	Healthy group had significant better performance on Word pair recall test than aMCI group [66% and 32%, respectively, F(1,22)= 15.6, p<.001], The test time × groups interaction was significant [F(1,22)= 9.6, p<.01]. In healthy group, the recall results were significant better after sleep than before sleep [t(15)= 2.2, p<.05]. In the aMCI group, the recall results were poorer after sleep than before sleep [t(7)= 3.4, p<.05]. The healthy group had better result of Fact Recognition

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					than did the aMCI group [56% and 23%, respectively, F(1, 22)= 17.3, p<.001]. In healthy group, the result of fact recognition was better after sleep than before sleep [t (15) = 2.9, p<.05] but the aMCI group did not (p=.8). In overall sample, the result of object priming was better after sleep than before sleep [F(1, 22) = 10.0, p<.005]. The aMCI group had significantly fewer minutes and proportion of SWS than did the healthy group [t (22) = 2.8, p<.05 and t(22)= 2.7, p<.05, respectively]. The ratio of SWS minutes to

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					REM minutes was significant smaller in the aMCI group than in the healthy group [0.007 vs. 0.12, respectively; t(22)= 2.6, p<.05]. For sleep-related brain waves, the aMCI group had significant reductions of delta and theta waves in NREM sleep than the healthy group [t(22)= 2.3, p<.05 and t(22)= 2.2, p<.05, respectively]. During REM sleep, the aMCI group had a significant reduction of theta wave than did the healthy group [t(22)= 2.9, p<.05]. For the relationship between sleep parameters and episodic memory tests, no sleep parameters were significantly correlated

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					with test results of episodic memory. For the relationship between sleep-related brain waves and episodic memory, on the first night, in overall sample, recall test results were significantly correlated with delta wave ($r=0.51$, $p<.05$) and theta wave ($r=0.49$, $p<.05$) in NREM sleep. On first night, in overall sample, recall test results were significantly correlated with delta wave ($r=0.56$, $p<.01$) and theta wave($r=0.60$, $p<.01$) in REM sleep. In healthy group, on the first night, recall test results was significantly

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					correlated with delta wave (r=0.54, p<.05) and theta wave (r=0.55, p<.05) in whole sleep. On the second night, among overall sample, recall test results were significantly correlated with delta wave (r=0.45, p<.05) and theta wave (r=0.53, p<.01) in NREM sleep. On the second night, in overall sample, recall test results were significantly correlated with delta wave (r=0.51, p<.05) and theta wave (r=0.68, p<.01) in REM sleep.
Hot et al.	2011	Unmedicated AD patients (n=14, mean age: 76.7 ± 3.8,	Cross-sectional	Sleep: PSG; Episodic memory: original task from	The AD patients had lower sleep efficiency than the healthy older adults [mean ± SD: 81± 10 vs.72± 10, t(26) = -2.09, p<.05].

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
		men/women: 7/7) vs. health older adults (n= 14, mean age: 76.7 ± 4.1, men/women: 6/8)		Grober and Buschke's procedure	In the AD patients, the faster theta rhythm during sleep was positively correlated with delayed cued recall of episodic memory (r=0.64, p<.05) and negatively correlated with forgetting rates (r=-0.64, p<.05).
Westerberg et al.	2010	aMCI patients (n= 10, mean age: 71.1, men/women: 2/8) and healthy older adults (n= 10, mean age: 72.5, men/women: 3/7)	Longitudinal	Sleep: wrist actigraphy for continuous 14 nights, PSQI and ESS, Karolinska Sleep Diary;	In aMCI patients, the time in bed (r = 0.2, p<.05) and fragmentation index (r = 0.31, p<.05) from an actigraphy and waking time (r = 0.23,p<.05), self-reported sleep assessment (r = 0.29, p<.05), self-reported sleep efficiency (r = 0.44, p<.05), and self- reported sleep difficulty in (r = -0.13, p<.05) from

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				Episodic memory: Warrington Recognition Memory test, Word-list learning and Recognition, Logical Memory and Visual Reproduction subset of Wechsler Memory Scale-Revised	Karolinska Sleep Diary were significantly correlated with the 24-hour recognition test. These correlations did not show in control group. For both aMCI patients and healthy older adults, variability of the time in bed ($r = -0.48$, $p<.05$), total sleep time ($r = -0.53$, $p<.05$), sleep latency ($r = -0.49$, $p<.05$), and sleep fragmentation ($r = -0.50$, $p<.05$) from actigraphy were significantly correlated with the Logical Memory subscale. The response of "whether participants slept through the time in bed" was correlated with lower recall rate ($r = -0.48$, $p<.05$). In aMCI patients and

(continued)

Table 2.3

Author	Years	Sample	Design	Measure	Results
				subsection in day one, continuous recognition test (tested by immediate recall and short-delayed recall) and 24-hour recognition test for next 14 days)	healthy older adults, the bed time [t(9)= 3.02, p<.05 and t(9)=3.60, p<.01, respectively], wake time [t(9)= 4.60, p<.005 and t(9)= 3.93, p<.005], and sleep time [t(9)=3.64, p<.01 and t(9)=6.48, p<.001] from sleep diary and actigraphy were significantly correlated with each other. Among aMCI patients, the result of the question of "what time did you arise this morning?" was positively correlated with wake time [t(9)= 4.85, p<.001], sleep end [t(9)= 5.84, p<,001], time in bed [t(9)= 4.02, p<.01], and total sleep time [t(9)= 3.76, p<.01] from actigraphy; the result of "Did you

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
					sleep throughout the allotted for sleep?" was positively correlated with wake time [t(9)=2.48, p<.05] and sleep start [t(9)= 2.46, p<.05] from the actigraphy; the result of the question of "How did you sleep?" was positively correlated with wake time [t(9)=4.75, p<.01] and sleep end [t(9)=2.96, p<.05] from the actigraphy.
Bonanni et al.	2005	Mild AD patients (n=11, mean age: 65.6 ± 7.4, men/women: 5/6), moderate AD patients (n= 9, mean	Cross-sectional	Sleep: PSG; Daytime sleepiness: multiple sleep latency test;	The mean score from multiple sleep latency test was significantly lower in moderate AD patients (9.79 ± 2.42) when compared with mild AD patients (12.14 ± 2.4) (p<.05) and healthy older adults (14.22 ±2.11) (p<.05) and

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
		age: 64 ± 8.7, men/women: 4/5), and healthy older adults (n= 12, mean age:61.1 ± 5.1, men /women: 7/5)		Episodic memory: verbal digital span and story recall	it was significantly lower in mild AD group when compared with healthy older adults ($p<.05$). Among the entire AD patients, the result of multiple sleep latency test was significantly and strongly correlated with verbal digit span ($r=0.56$, $p<.05$) and story recall ($r=0.67$, $p<.05$).
Non-randomized controlled experimental					
Van Der Werf et al.	2011	Healthy older adults without sleep disturbances (n= 13, mean age: 60.1 ± 8.3, men/women: 4/9).	Cross-over design, cross-sectional	Sleep: artificially disrupted SWS under the screen of PSG to measure reduced	Compared to a night with normal sleep, after the night of slow wave activity reduction by SWS disruption, the participants did have lower scores on true positive response (normal sleep: mean± SD, 36.6 ± 1.4 items, SWA

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
		All of them experience a normal sleep night and a SWS-disrupted night		slow wave activity for 2 consecutive nights and normal sleep; Episodic memory: 50 unfamiliar landscape pictures and then received one day delayed recognition test by recognizing 50 presented pictures	reduction: 31.4 ± 1.8 item; p=.008). The subjects after SWS disrupted night had a significantly lower d-prime than after normal sleep (normal sleep: mean ± SD, 1.07 ± 0.09 items; SWA reduction: 0.7 ± 0.06 items, p =.007). Compared with in normal sleep, the subjects in slow wave activity reduction condition had a significant reduction of right hippocampal activity. The p-value was not reported.

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
Stenuit et al.	2008	Health young women (n= 10, mean age: 23.2 ± 7.5); healthy older women (n= 10, mean age: 60 ± 3.7)	Cross-sectional	The subjects followed a sleep-wake schedule: one baseline night (8hours), 3 continuous sleep restriction nights (4hours), one recovery night (8hours); Sleep: PSQI, ESS, actigraphy , PSG;	The free recall rates of Buschke test including first immediate and delayed recall during sleep restriction was significantly lower than in normal sleep for both groups [$F(4, 72) = 7.031$, $p<.01$].

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				Episodic memory: Buschke 16 items including 3 immediate recall and one delayed recall, logical memory, Paced Auditory serial task, Brown Peterson test, Addition of numbers	

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
Fenn et al.	2009	Adults (N= 92) divided into two groups: 12-hour break with sleep group (n= 46) and 12-hour break without sleep group (n= 46) after learning task	Cross-sectional	Episodic memory: recognition test to determine learned and unlearned words within a 15-word list	Compared to the group with 12-hour break not including sleep, the group with 12-hour break including sleep had fewer false recognition for unlearned word [$t(61) = 2.03$ $p < .05$], fewer false recognition of critical lures [$t(30) = 2.78$ $p < .01$], fewer remember responses to critical lures [$t(90) = 2.41$ $p < .01$], fewer false recognition of critical lures [$t(90) = 2.0$ $p < .05$; $t(61) = 2.2$ $p < .05$], and fewer recognition of list words from unstudied lists [$t(61) = 2.7$ $p < .01$].

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
			Randomized controlled experimental		
Backhaus et al.	2007	Healthy younger adults (n= 16, mean age: 20.4 ± 0.6); healthy middle-age adults (n= 14, mean age: 50.0 ± 0.6).	Cross-sectional	All participants in each age group were randomly assigned into two experimental nights: early and late sleep; Sleep: PSG; Tiredness: SSS; Declarative memory: word-pair associate task consisting of 40	After early sleep conditions, the young group retained a significantly greater numbers of learned word pairs than the middle-age group [mean ± SD: 34.8 ± 0.8 in young group and 29.2 ± 1.0 in middle-age group, t (28) = 4.29, p<.001). After late sleep condition, the young group retained more number of learned word pairs than the middle-age group [mean ± SD: 32.3 ± 1.0 in young group and 27.0 ± 1.8 in middle-age group, t (28) =2.51, p =0.02].Only the time of SWS was a significant predictor of retention rate of word pairs (β =0.51, p<.05)

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Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
				word pairs of German nouns.	in all participants. R^2 value was not reported. Retention of word-pairs was worse in late sleep condition compared to with early sleep condition [F(1.28) = 9.2, p=0.005]. The retention of word-pair was significantly correlated to the percentage of SWS during early sleep (r= 0.51, p=.004).
Hornung et al.	2007	Healthy old adults (N=107, mean ages: 66.1 ± 5.1, men/women: 52/55). All subjects were divided into 5	Experimental, cross-sectional	Sleep: PSG; Episodic memory: cue recall test of a list of 34 word pairs including three recall trials	The number of errors in a declarative memory test was significantly lower in the test after sleep than before sleep in all experimental groups (p<.001). However, this improvement did not significantly correlate to any sleep parameters. The results of a declarative

(continued)

Table 2.3 (continued)

Author	Years	Sample	Design	Measure	Results
		experimental groups: selective REM sleep deprivation (n=24), stage 2 NREM sleep awakening (n= 20), REM rebound (n= 21), REM augmentation by AChE-I (n= 22), and control group (n=20).		before and after study night	memory test did not differ between each experimental group.

Note. PSG= polysomnograph; SSS= Stanford sleepless score; PSQI= Pittsburgh Sleep Quality Index; CI= confidence interval; OR= odds ratio; SD=standard deviation; WMS= Wechsler Memory Scale; AD= Alzheimer's Disease; REM= rapid eye movement; SWS= slow wave sleep; NREM= non-rapid eye movement; ESS: Epworth Sleepiness Scale; aMCI= amnesiac mild cognitive impairment; MCI= mild cognitive impairment; MMSE= mini–mental state examination; DM= diabetes; fMRI= Functional magnetic resonance imaging; AchEI= Acetylcholinesterase Inhibitor.

Table 2.4

The Comparison of Association between Similar Sleep Characteristics and Episodic Memory in terms of Different Measures

Sleep characteristics	Measurement	Studies	Results
Total sleep time	PSG	Hart et al. (1995)	The performance of episodic memory was explained by the total sleep time (R^2 = 0.13, F=10.8, p<.01).
	Self-reported	Kronholm et al. (2009) Tworoger et al. (2006) Ferrie et al. (2011) Xu et al., (2011) Loerbroks et al. (2010)	Total sleep time had a reverse U-shape association with episodic memory with a peak at 7-8 hours (p<.05). Among shorter sleepers (total sleep time ≤ 6 hours), total sleep time was positive correlated with the episodic memory (r=0.16 ~0.10, p<.05) or had higher risk of poor performance of episodic memory (OR: 1.53~1.29, p<.05). Among longer sleepers (total sleep time ≥ 9 hours), total sleep time was negatively correlated with episodic memory in older adults (r = -0.21, p<.05) and significantly higher risk of poor episodic memory (OR: 1.52, p<.001). The older adults with increased sleep time (7 or 8 hours to ≥ 9 hours) had two-fold higher prevalence of poor

(continued)

Table 2.4 (continued)

Sleep characteristics	Measurement	Studies	Results
Total sleep time	Self-reported	Schmutte et al. (2007)	episodic memory (PR= 1.98, 95% CI: 1.04-3.78). Older adults with ≤ 4 hours sleep and > 9 hours sleep had significant poor episodic memory than the group with 5-6 hours and 7-8 hours sleep (p=.01 to .009).
	St. Mary's Hospital Sleep Questionnaire	Aly & Moscovitch (2010)	The total sleep time in the older adults was significantly correlated with the episodic memory benefit from sleep (r=0.78, p=.008).
	14-day wrist actigraphy	Westerberg et al. (2010)	Total sleep time was negatively correlated with the result of episodic memory test in older adults (r=-0.53, p<.05).
	7-day wrist worn actigraphy	Cochrane et al. (2012)	Total sleep time was significantly correlated with the result of episodic memory test (r=-0.53, p<.05).

(continued)

Table 2.4 (continued)

Sleep characteristics	Measurement	Studies	Results
Sleep latency and sleep fragmentation	Self-reported	Tworoger et al. (2006)	Compared with the participant who rarely or never had difficulty in falling asleep or staying sleep, women who reported that they regularly had difficulty in falling or staying asleep had an increased risk of episodic memory (OR: 1.45, 95% CI: 0.74, 2.85).
		Gamaldo et al. (2008)	Problem of falling asleep did not significantly correlated with episodic memory (r=-0.03, p>.05).
		Schmutte et al. (2007)	Older adults with longer sleep latency particularly exceed 30 minutes had significantly poor episodic memory than the group with shorter sleep onset latency (p=.007 to.001)
		Westerberg et al. (2010)	The response of "whether participants slept through the time in bed" was negatively correlated to episodic memory function (r=-0.48, p<.05).

(continued)

Table 2.4 (continued)

Sleep characteristics	Measurement	Studies	Results
Sleep latency and sleep fragmentation	14-day wrist actigraphy	Westerberg et al. (2010)	Sleep latency ($r=-0.49$, $p<.05$), and sleep fragmentation ($r=-0.50$, $p<.05$) from actigraphy were significantly and negatively correlated to the result of logical memory.
Daytime sleepiness	Multiple sleep latency test	Bonanni et al. (2005)	Among the entire AD patients, the result of multiple sleep latency test was significantly correlated to story recall ($r=0.67$, $p<.05$). The higher the level of daytime sleepiness, the poorer the episodic memory function.
	sleep-EVAL system	Ohayon et al. (2002)	Compared with the participants who took intentional nap and never took nap, the participants who took unintentional naps had higher scores of difficulty in delayed recall (1.63 ± 2.05 in unintentional nap vs. 0.73 ± 1.58 in never nap, 0.74 ± 1.46 in intentional nap group, $p<.05$). Daytime sleepiness was a predictor of the result of episodic memory test (OR: 2.0, 95% CI, 1.3-3.0, $P<.01$).

(continued)

Table 2.4 (continued)

Sleep characteristics	Measurement	Studies	Results
Daytime sleepiness	Self-reported	Xu et al., (2011)	The increase in the frequency of daytime napping was significantly association with decline of episodic memory (p-value for trend =.005). Compared to the group who never felt tired in the morning or feel tired less than in 1day/week, the group who felt tired in the morning in 1-2 days/ week [OR: 1.18(CI: 1.01-1.39) p=.04] or in almost daily [OR: 1.27 (CI: 1.05-1.53), p=.01] had significant risk for poorer performance in episodic memory. The increase in frequency of morning tiredness was significantly associated with decrease in episodic memory (p-value for trend<.001). The group felt tiredness daily had poorer performance in episodic memory test than the group who never or less than 1-2 days/week felt tiredness in the morning (p<.001).

(continued)

Table 2.4 (continued)

Sleep characteristics	Measurement	Studies	Results
Daytime sleepiness	Self-reported	Kronholm et al. (2009)	Feeling of "fatigue and tiredness" was associated consistently and linearly with decreased rate to report " very good" or " good" in self-assessment of memory.
SWS	PSG	Van Der Werf et al. (2011)	Compared to normal sleep night, after the night of slow wave activity reduction by SWS disruption, the subjects did have poorer performance on episodic memory test (normal sleep: mean$\pm$ SD, 36.6 ± 1.4 items, SWA reduction: 31.4 ± 1.8 item; p=.008).
		Backhaus et al. (2007)	The time of SWS was a significant predictor of retention rate of word pairs (β =0.51, p=0.004) in young and older participants and episodic memory was significantly correlated to the percentage of SWS during early sleep (r=0.51, p=.004).

(continued)

Table 2.4 (continued)

Sleep characteristics	Measurement	Studies	Results
SWS	PSG	Westerberg et al. (2012)	The aMCI group had significantly fewer minutes and proportion of SWS than did the healthy group [$t(22)= 2.8$, $p<.05$ and $t(22)= 2.7$, $p<.05$, respectively]. The ratio of SWS minutes to REM minutes was significant smaller in the aMCI group than in the healthy group [0.007 vs. 0.12, respectively; $t(22)= 2.6$, $p<.05$].

Note. PSG= polysomnograph; SWS= slow wave sleep; AD= Alzheimer's disease

References

Aly, M., & Moscovitch, M. (2010). The effects of sleep on episodic memory in older and younger adults. *Memory, 18*(3), 327-334.

Backhaus, J., Born, J., Hoeckesfeld, R., Fokuhl, S., Hohagen, F., & Junghanns, K. (2007). Midlife decline in declarative memory consolidation is correlated with a decline in slow wave sleep. *Learning & Memory, 14*(5), 336-341. doi:14/5/336

Beaudreau, S. A., & O'Hara, R. (2009). The association of anxiety and depressive symptoms with cognitive performance in community-dwelling older adults. *Psychology and Aging, 24*(2), 507-512.

Beaunieux, H., Hubert, V., Pitel, A. L., Desgranges, B., & Eustache, F. (2009). Episodic memory deficits slow down the dynamics of cognitive procedural learning in normal ageing. *Memory, 17*(2), 197-207. doi:10.1080/09658210802212010

Blackwell, T., Yaffe, K., Ancoli-Israel, S., Redline, S., Ensrud, K. E., Stefanick, M. L., . . . Osteoporotic Fractures in Men (MrOS) Study Group. (2011). Association of sleep characteristics and cognition in older community-dwelling men: The MrOS sleep study. *Sleep, 34*(10), 1347-1356. doi:10.5665/SLEEP.1276

Bliwise, D. L., Friedman, L., & Yesavage, J. A. (1993). Depression as a confounding variable in the estimation of habitual sleep time. *Journal of Clinical Psychology, 49*(4), 471-477.

Bonanni, E., Maestri, M., Tognoni, G., Fabbrini, M., Nucciarone, B., Manca, M. L., . . . Murri, L. (2005). Daytime sleepiness in mild and moderate Alzheimer's disease and its relationship with cognitive impairment. *Journal of Sleep Research, 14*(3), 311-317.

Burton, C. L., Strauss, E., Hultsch, D. F., & Hunter, M. A. (2006). Cognitive functioning and everyday problem solving in older adults. *The Clinical Neuropsychologist, 20*(3), 432-452.

Cansino, S. (2009). Episodic memory decay along the adult lifespan: A review of behavioral and neurophysiological evidence. *International Journal of Psychophysiology, 71*(1), 64-69.

Cochrane, A., Robertson, I. H., & Coogan, A. N. (2012). Association between circadian rhythms, sleep and cognitive impairment in healthy older adults: An actigraphic study. *Journal of Neural Transmission, 119*(10), 1233-1239.

Dickerson, B. C., & Eichenbaum, H. (2010). The episodic memory system: Neurocircuitry and disorders. *Neuropsychopharmacology : Official Publication of the American College of Neuropsychopharmacology, 35*(1), 86-104. doi:10.1038/npp.2009.126

Edwards, B. A., O'Driscoll, D. M., Ali, A., Jordan, A. S., Trinder, J., & Malhotra, A. (2010). Aging and sleep: Physiology and pathophysiology. *Seminars in Respiratory and Critical Care Medicine, 31*(5), 618-633. doi:10.1055/s-0030-1265902

Ellenbogen, J. M., Hulbert, J. C., Jiang, Y., & Stickgold, R. (2009). The sleeping brain's influence on verbal memory: Boosting resistance to interference. *PLoS One, 4*(1), e4117.

Ensrud, K. E., Blackwell, T. L., Redline, S., Ancoli-Israel, S., Paudel, M. L., Cawthon, P. M., . . . Stone, K. L. (2009). Sleep disturbances and frailty status in older community-dwelling men. *Journal of the American Geriatrics Society, 57*(11), 2085-2093.

Espiritu, J. R. D. (2008). Aging-related sleep changes. *Clinics in Geriatric Medicine, 24*(1), 1-14.

Fenn, K. M., Gallo, D. A., Margoliash, D., Roediger, H. L.,3rd, & Nusbaum, H. C. (2009). Reduced false memory after sleep. *Learning & Memory, 16*(9), 509-513. doi:10.1101/lm.1500808

Ferrie, J. E., Shipley, M. J., Akbaraly, T. N., Marmot, M. G., Kivimaki, M., & Singh-Manoux, A. (2011). Change in sleep duration and cognitive function: Findings from the Whitehall II study. *Sleep, 34*(5), 565-573.

Ficca, G., Lombardo, P., Rossi, L., & Salzarulo, P. (2000). Morning recall of verbal material depends on prior sleep organization. *Behavioural Brain Research, 112*(1), 159-163.

Foley, D. J., Monjan, A. A., Brown, S. L., & Simonsick, E. M. (1995). Sleep complaints among elderly persons: An epidemiologic study of three communities. *Sleep: Journal of Sleep Research & Sleep Medicine,*

Fotuhi, M., Do, D., & Jack, C. (2012). Modifiable factors that alter the size of the hippocampus with ageing. *Nature Reviews Neurology, 8*(4), 189-202.

Gagnon, K., Baril, A. A., Gagnon, J. F., Fortin, M., Décary, A., Lafond, C., ... Gosselin, N. (2014). Cognitive impairment in obstructive sleep apnea. *Pathologie Biologie, 62*(5), 233-240. doi:10.1016/j.patbio.2014.05.015

Gamaldo, A. A., Allaire, J. C., & Whitfield, K. E. (2008). The relationship between reported problems falling asleep and cognition among African American elderly. *Research on Aging, 30*(6), 752-767.

Goldberg, T. E., Koppel, J., Keehlisen, L., Christen, E., Dreses-Werringloer, U., Conejero-Goldberg, C., . . . Davies, P. (2010). Performance-based measures of everyday function in mild cognitive impairment. *The American Journal of Psychiatry, 167*(7), 845-853. doi:10.1176/appi.ajp.2010.09050692

Gonzalez, H. M., Bowen, M. E., & Fisher, G. G. (2008). Memory decline and depressive symptoms in a nationally representative sample of older adults: The health and retirement

study (1998-2004). *Dementia and Geriatric Cognitive Disorders, 25*(3), 266-271. doi:10.1159/000115976

Grimes, D. A., & Schulz, K. F. (2002). An overview of clinical research: The lay of the land. *The Lancet, 359*(9300), 57-61.

Haimov, I. (2006). Association between memory impairment and insomnia among older adults. *European Journal of Ageing, 3*(2), 107-115.

Hart, R. P., Morin, C. M., & Best, A. M. (1995). Neuropsychological performance in elderly insomnia patients. *Aging, Neuropsychology, and Cognition, 2*(4), 268-278.

Hornung, O. P., Regen, F., Danker-Hopfe, H., Schredl, M., & Heuser, I. (2007). The relationship between REM sleep and memory consolidation in old age and effects of cholinergic medication. *Biological Psychiatry, 61*(6), 750-757.

Hot, P., Rauchs, G., Bertran, F., Denise, P., Desgranges, B., Clochon, P., & Eustache, F. (2011). Changes in sleep theta rhythm are related to episodic memory impairment in early Alzheimer's disease. *Biological Psychology, 87*(3), 334-339.

Hu, P., Stylos-Allan, M., & Walker, M. P. (2006). Sleep facilitates consolidation of emotional declarative memory. *Psychological Science, 17*(10), 891-898. doi:PSCI1799

Kronholm, E., Sallinen, M., Suutama, T., Sulkava, R., Era, P., & Partonen, T. (2009). Self-reported sleep duration and cognitive functioning in the general population. *Journal of Sleep Research, 18*(4), 436-446.

Lahl, O., & Pietrowsky, R. (2007). The long range effect of sleep on episodic memory. *Sleep and Hypnosis, 9*(1), 24.

Lavery, L. L., Dodge, H. H., Snitz, B., & Ganguli, M. (2009). Cognitive decline and mortality in a community-Based cohort: The Monongahela valley independent elders survey. *Journal of the American Geriatrics Society, 57*(1), 94-100.

Lee, H. B., Kasper, J. D., Shore, A. D., Yokley, J. L., Black, B. S., & Rabins, P. V. (2006). Level of cognitive impairment predicts mortality in high-risk community samples: The memory and medical care study. *The Journal of Neuropsychiatry and Clinical Neurosciences, 18*(4), 543-546. doi:10.1176/appi.neuropsych.18.4.543

Lo, J., Loh, K., Zheng, H., Sim, S., & Chee, M. (2014). Sleep duration and age-related changes in brain structure and cognitive performance. *Sleep, 37*(7), 1171-1178.

Loerbroks, A., Debling, D., Amelang, M., & Stürmer, T. (2010). Nocturnal sleep duration and cognitive impairment in a population-based study of older adults. *International Journal of Geriatric Psychiatry*, *25*(1), 100-109.

Maglione, J. E., Ancoli-Israel, S., Peters, K. W., Paudel, M. L., Yaffe, K., Ensrud, K. E., & Stone, K. L. (2012). Depressive symptoms and subjective and objective sleep in Community-Dwelling older women. *Journal of the American Geriatrics Society, 60*(4), 635-643.

Martin, J. L., Fiorentino, L., Jouldjian, S., Josephson, K. R., & Alessi, C. A. (2010). Sleep quality in residents of assisted living facilities: Effect on quality of life, functional status, and depression. *Journal of the American Geriatrics Society, 58*(5), 829-836.

Mazzoni, G., Gori, S., Formicola, G., Gneri, C., Massetani, R., Murri, L., & Salzarulo, P. (1999). Word recall correlates with sleep cycles in elderly subjects. *Journal of Sleep Research, 8*(3), 185-188.

Merritt, P., Hirshman, E., Zamani, S., Hsu, J., & Berrigan, M. (2006). Episodic representations support early semantic learning: Evidence from midazolam induced amnesia. *Brain and Cognition, 61*(2), 219-223. doi:10.1016/j.bandc.2005.12.001

Nebes, R. D., Buysse, D. J., Halligan, E. M., Houck, P. R., & Monk, T. H. (2009). Self-reported sleep quality predicts poor cognitive performance in healthy older adults. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 64*(2), 180-187. doi:10.1093/geronb/gbn037

Ohayon, M. M., & Vecchierini, M. (2002). Daytime sleepiness and cognitive impairment in the elderly population. *Archives of Internal Medicine, 162*(2), 201-208.

Oosterman, J. M., van Someren, E. J., Vogels, R. L., van Harten, B., & Scherder, E. J. (2009). Fragmentation of the rest-activity rhythm correlates with age-related cognitive deficits. *Journal of Sleep Research, 18*(1), 129-135.

Panza, F., D'Introno, A., Colacicco, A. M., Capurso, C., Del Parigi, A., Caselli, R. J., . . . Scafato, E. (2009). Temporal relationship between depressive symptoms and cognitive impairment: The italian longitudinal study on aging. *Journal of Alzheimer's Disease, 17*(4), 899-911.

Poe, G. R., Walsh, C. M., & Bjorness, T. E. (2010). Cognitive neuroscience of sleep. In G. A. Kerkhof & H. P. A. Van Dongen (Eds.), *Progress in brain research*: Vol. 185. (pp. 1-19). doi:10.1016/B978-0-444-53702-7.00001-4

Rauchs, G., Bertran, F., Guillery-Girard, B., Desgranges, B., Kerrouche, N., Denise, P., . . . Eustache, F. (2004). Consolidation of strictly episodic memories mainly requires rapid eye movement sleep. *Sleep: Journal of Sleep and Sleep Disorders Research,*

Rauchs, G., Desgranges, B., Foret, J., & Eustache, F. (2005). The relationships between memory systems and sleep stages. *Journal of Sleep Research, 14*(2), 123-140.

Rauchs, G., Schabus, M., Parapatics, S., Bertran, F., Clochon, P., Hot, P., . . . Anderer, P. (2008). Is there a link between sleep changes and memory in Alzheimer's disease? *Neuroreport, 19*(11), 1159-1162. doi:10.1097/WNR.0b013e32830867c4

Schmutte, T., Harris, S., Levin, R., Zweig, R., Katz, M., & Lipton, R. (2007). The relation between cognitive functioning and self-reported sleep complaints in nondemented older adults: Results from the bronx aging study. *Behavioral Sleep Medicine, 5*(1), 39-56.

Spencer, R. M., Gouw, A. M., & Ivry, R. B. (2007). Age-related decline of sleep-dependent consolidation. *Learning & Memory, 14*(7), 480-484. doi:14/7/480

Spira, A. P., Gamaldo, A. A., An, Y., Wu, M. N., Simonsick, E. M., Bilgel, M., . . . Resnick, S. M. (2013). Self-reported sleep and beta-amyloid deposition in community-dwelling older adults. *JAMA Neurology, 70*(12), 1537-1543. doi:10.1001/jamaneurol.2013.4258

Squire, L.R., & Kandel, E. R. (2009). *Memory: from Mind to Molecules*. Greenwood Village, CO: Roberts and Company Publishers

Stenuit, P., & Kerkhofs, M. (2008). Effects of sleep restriction on cognition in women. *Biological Psychology, 77*(1), 81-88.

Sutter, C., Zöllig, J., Allemand, M., & Martin, M. (2012). Sleep quality and cognitive function in healthy old age: The moderating role of subclinical depression. *Neuropsychology, 26*(6), 768.

Tworoger, S. S., Lee, S., Schernhammer, E. S., & Grodstein, F. (2006). The association of self-reported sleep duration, difficulty in sleep, and snoring with cognitive function in older

women. *Alzheimer Disease and Associated Disorders, 20*(1), 41-48. doi:10.1097/01.wad.0000201850.52707.80

Van Der Werf, Y. D., Altena, E., Vis, J. C., Koene, T., & Van Someren, E. J. W. (2011). Chapter 16 - Reduction of nocturnal slow-wave activity affects daytime vigilance lapses and memory encoding but not reaction time or implicit learning. In G. A. Kerkhof & H. P. A. Van Dongen (Eds.), *Progress in brain research*: Vol.193, (pp. 245-255). doi:10.1016/B978-0-444-53839-0.00016-8

Westerberg, C. E., Mander, B. A., Florczak, S. M., Weintraub, S., Mesulam, M., Zee, P. C., & Paller, K. A. (2012). Concurrent impairments in sleep and memory in amnestic mild cognitive impairment. *Journal of the International Neuropsychological Society, 18*(03), 490-500.

Westerberg, C. E., Lundgren, E. M., Florczak, S. M., Mesulam, M. M., Weintraub, S., Zee, P. C., & Paller, K. A. (2010). Sleep influences the severity of memory disruption in amnestic mild cognitive impairment: Results from sleep self-assessment and continuous activity monitoring. *Alzheimer Disease and Associated Disorders, 24*(4), 325-333. doi:10.1097/WAD.0b013e3181e30846

Wilson, J. K., Baran, B., Pace-Schott, E. F., Ivry, R. B., & Spencer, R. (2012). Sleep modulates word-pair learning but not motor sequence learning in healthy older adults. *Neurobiology of Aging, 33(5), 991-1000.*

Xu, L., Jiang, C. Q., Lam, T. H., Liu, B., Jin, Y. L., Zhu, T., . . . Thomas, G. N. (2011). Short or long sleep duration is associated with memory impairment in older Chinese: The Guangzhou Biobank cohort study. *Sleep, 34*(5), 575-580.

Yoo, S., Hu, P. T., Gujar, N., Jolesz, F. A., & Walker, M. P. (2007). A deficit in the ability to form new human memories without sleep. *Nature Neuroscience, 10*(3), 385-392.

Zimmerman, M. E., Bigal, M. E., Katz, M. J., Brickman, A. M., & Lipton, R. B. (2012). Sleep onset/maintenance difficulties and cognitive function in nondemented older adults: The role of cognitive reserve. *Journal of the International Neuropsychological Society*, *18*(3), 461-470.

Chapter Three

How Does Self-reported Sleep Disturbances Relate to Objectively Measured Sleep in Older Adults?

Abstract

Introduction: Sleep disturbances are a common problem in the aging population. Around 50% of older adults over 65 years of age have chronic sleep disturbances. The multidimensionality of sleep disturbances in older adults is supported by various measurements of this problem, including self-reported questionnaires and objective measures (e.g., actigraphy and polysomngraph). In prior literature, the association between self-reported and objectively measured sleep disturbances was unclear. The purpose of this study was to investigate the relationship between self-reported and objectively measured sleep disturbances among older adults.

Method: Data were obtained from 62 older adults who were over 60 years of age (male: 24.2%; mean age: 69.9; education years: 18.17). Self-reported sleep disturbances were measured by the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and sleep logs. Higher PSQI and ESS scores indicate poorer sleep quality and more daytime sleepiness, respectively. Objective sleep parameters were measured by actigraphy. Participants wore an actigraph device on the non-dominant wrist continuously for 7 days. Descriptive statistics, Pearson's correlation, and multiple regression analyses were conducted. Exploratory factor analysis was used to explore the factor structure among physical sleep parameters from actigraphy and to reduce data.

Principle component method was used to extract factors; eigenvalues over the Kaiser's criterion of >1 and scree plot were used to determine factor numbers; and the Varimax method was used to rotate factor loading.

Results: The results of Pearson's correlation showed that objective wakefulness during sleep periods was correlated with self-reported sleep time ($r= -0.27$, $p<.05$), sleep efficiency ($r= -0.46$, $p<.01$), and total PSQI score ($r=0.35$, $p<.01$). Objective sleep time was correlated with self-reported sleep time ($r=0.51$, $p<.01$) and napping time ($r= -0.27$, $p<.05$) in older adults. Objective difficulty in falling and staying asleep were not significantly correlated with self-reported sleep problems. The multiple regression results showed that self-reported sleep parameters including self-reported sleep time, sleep latency, sleep efficiency, and total PSQI score, total ESS score, and napping time can significantly explain objective sleep time [$R^2= 0.69$, $F (6, 55)= 20.34$, $p=.000$], and objective wakefulness during sleep periods [$R^2= 0.24$, $F (6, 55)= 2.81$, $p=.019$] after controlling for covariates (i.e., gender, healthy condition, and depressive symptoms).

Conclusion: These results showed that only self-reported sleep parameters substantially predicted objective sleep time rather than wakefulness during sleep periods and difficulties for falling and staying asleep, which are the most frequent symptoms of sleep disorders (i.e., sleep apnea and insomnia) after excluding the influence of related factors (i.e., gender, healthy conditions, and depressive symptoms). These results suggest that in future sleep studies of older adults, the selection of sleep measures needs to be based on the purpose of the study to fully understand sleep problems.

Introduction

Sleep disturbances are a common problem in the aging population, with around 50% of community-dwelling older adults over 65 years of age having this problem (Blackwell et al., 2011; Foley et al., 1995). Older adults suffer from a number of characteristics of sleep disturbances that have been self-reported or objectively measured (Blackwell et al., 2011; Edwards et al., 2010; Ensrud et al., 2009; Espiritu, 2008). The characteristics of sleep disturbances are shown in Table 3.1.

Sleep disturbances are a multidimensional problem, which can be identified by various measures, including self-reported questionnaires and objective measures (e.g., actigraphy and polysomngraph). Among self-reported questionnaires, different questionnaires measure different dimensions of sleep disturbances. For instance, sleep quality has been evaluated by the Pittsburgh Sleep Quality Index (PSQI) (Beaudreau et al., 2012; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989; Spira et al., 2012) and daytime sleepiness has been identified by the Epworth Sleepiness Scale (ESS) (Johns, 1991). Although the results of these two questionnaires are correlated (Spira et al., 2012), they measure different dimensions of sleep disturbances. Due to the limitations of self-reported questionnaires, objective measures are commonly used in sleep studies. Among objective measures of sleep disturbances, actigraphy has been used to measure sleep (Cole, Kripke, Gruen, Mullaney, & Gillin, 1992). The data recorded by actigraphy when compared with time to bed and wakening can provide sleep characteristics of total sleep duration [the real total time asleep in the bed (Ensrud et al., 2009)], total bed time, sleep latency [the amount of minutes before sleep onset while in bed (Ensrud et al., 2009)], sleep efficiency [the ratio of total sleep duration to total bed time by percentage (Ensrud et al., 2009)], total length, average length, and number of wakefulness after sleep onset (WASO), and average length and

number of long wakefulness after sleep onset (LWASO) [fragmented sleep episodes > 5 min (Ensrud et al., 2009)]. Despite the availability of these data, few studies that evaluated the factor structure and interrelationships among these sleep parameters.

Some studies have investigated the association between self-reported and objective sleep disturbances of older adults. For example, in the study by Hart et al. (1995) of older adults (N=78), sleep efficiency and fragmented sleep reported in sleep diaries and recorded via polysomnography were significantly correlated with each other ($r=0.23$, $p<.05$ and $r=0.33$, $p<.01$, respectively) (Hart et al., 1995), but the magnitude of the correlation was weak.

The study by Vitiello and colleagues (2004) found that among older adults (N=150), the sleep parameters reported in the PSQI and recorded via polysomnography [total bed time ($r=0.44$, $p<.000$), total sleep duration ($r=0.29$, $p<.000$), total wake time ($r=0.27$, $p <.001$), sleep efficiency ($r=0.24$, $p<.003$), and sleep latency ($r=0.16$, $p<.05$)] were significantly correlated, but the magnitudes were low to medium. In addition to comparing correspondent sleep parameters reported in the PSQI and recorded via polysomnography, this study found differences in these sleep parameters. Compared with older adults who reported good sleep quality (the PSQI score ≤ 5), older adults who reported poor sleep quality (total PSQI score >5) had significantly poorer objective sleep characteristics including longer sleep latency ($p=.000$), longer total wake time ($p=.011$), lower sleep efficiency ($p=.005$). When the differences in objective sleep characteristics between the participants who had different self-reported sleep quality were further examined separately by gender, these differences were stronger among older men than older women. These results indicate an influence of gender in self-reported sleep estimations and objective sleep characteristics (Vitiello, Larsen, & Moe, 2004).

Following a similar design as Vitiello et al. (2004), McCrae and colleagues (2005) found different results among older adults. In their study, the sample (N=116) was divided into four groups based on the results of sleep diaries: non-complaining good sleepers, complaining good sleeper, non-complaining poor sleeper, and complaining poor sleepers. Among non-complaining good sleepers, total sleep duration obtained from a sleep diary and actigraphy was significantly and strongly correlated ($r= 0.84$, $p<.001$). This correlation was stronger among older women ($r=0.91$, $p<.001$) than among older men ($r=0.63$, $p<.01$). Among non-complaining poor sleepers, sleep latency ($r=0.81$, $p<.001$) and total sleep duration ($r=0.80$, $p<.001$) obtained from a sleep diary and actigraphy were significantly and strongly correlated. These correlations were stronger among older women (sleep latency: $r=0.88$, $p<.001$; total sleep duration: $r=0.80$, $p<.001$) than among older men (sleep latency: $r=0.59$, $p>.05$; total sleep duration: $r=0.92$, $p<.001$) (McCrae et al., 2005).

Additionally, Rotenberg and colleagues (2000) investigated the relationship between self-reported sleep parameters reported in a sleep questionnaire and objective sleep parameters recorded via polysomnography among depression patients and healthy control adults. The results showed that among all participants (N=40), objective sleep parameters measured via polysomnography were significantly correlated only with self-reported sleep duration, numbers of WASO, and sleep latency. However, these self-reported sleep parameters did not correlate with correspondent objective sleep parameters (i.e., self-reported sleep duration to objective sleep duration). Self-reported sleep duration was significantly correlated with percentage of slow wave sleep (Spearman rho=0.37, $p<.004$, Pearson $r=0.40$, $p<.002$) and the length of slow wave sleep in the second cycle (Spearman rho= 0.31, $p<.002$, Pearson $r=0.32$, $p<.01$). In only

health individuals (N=10), self-reported sleep duration was significantly correlated with the length of slow wave sleep in second sleep cycle (Spearman rho= 0.62, p<.003) (Rotenberg, Indursky, Kayumov, Sirota, & Melamed, 2000). These results suggest complexity in the relationship between self-reported and objectively measured sleep parameters. The correlations between them may be not only limited to corresponding self-reported and objectively measured sleep parameters.

Several factors such as gender, health conditions, and depression/depressive symptoms may influence self-reported sleep estimation and further influence self-reported and objective sleep parameters. Both of the studies by Vitiello et al. (2004) and McCrae et al. (2005) indicated that gender was a significant factor affecting the relationship between self-reported and objectively measured sleep parameters in older adults (McCrae et al., 2005; Vitiello et al., 2004), suggesting that women tend to more accurately estimate sleep than men. The study by McCrae et al. (2005) demonstrated that health conditions were associated with self-reported sleep estimation. Complaining good and poor sleepers had approximately 1 to 2 more chronic diseases than non-complaining good and poor sleepers had [F(3, 99)= 6.84, p<.001]. In addition to gender and health conditions, depression/depressive symptoms can affect self-reported sleep estimations (Rotenberg et al., 2000). The study by Rotenberg and colleagues (2000) showed that although both adults with and without depression tended to underestimate or overestimate sleep duration, adults with depression had a larger degree of overestimation (88.6 $\pm$ 32.7 vs. 50.0 $\pm$ 11.5 min, p<.001) and underestimation (-204$\pm$ 143.1 vs. -90.3 $\pm$ 46.2 min, p<.01) (Rotenberg et al., 2000). These related factors (i.e., gender, health conditions, depression) affecting older adults to estimate their sleep were controlled in current study.

Although in past studies, self-reported sleep parameters were correlated with objectively measured sleep parameters, it remains unclear whether self-reported and objectively measured sleep disturbances can explain or predict each other after controlling for related factors and whether the changes in sleep physiology can be observed by self-reported sleep complaint. Despite the availability of sleep parameters recorded via actigraphy, few studies have been done to determine the factor structure and interrelationships among these sleep parameters. Given this uncertainty, it is difficult to identify whether to use self-reported or objectively measured sleep data or both of them in order to understand sleep disturbances among older adults. Thus, the aims of this study were 1) to determine the factor structure of the different sleep parameters recorded via actigraphy and 2) to understand the association between self-reported and objectively measured sleep disturbances among older adults. The hypothesis of this study was that self-reported sleep parameters were significantly correlated with and able to explain objective sleep parameters recorded via actigraphy after controlling for covariates (i.e., gender, healthy condition, and depression) in older adults.

Method

Participants and Settings

This study was conducted using a descriptive design (Grimes & Schulz, 2002). Before initiating this study, approval from the Institutional Review Board (IRB) of University of Michigan was obtained. Following IRB approval, possible participants were recruited from the Michigan Alzheimer's Disease Center at Ann Arbor, Michigan and the database of the UMClinicalStudies.org website. Possible participants provided signed informed consents and then were screened to determine eligibility based on inclusion and exclusion criteria. The criteria for research participants to be included were (1) healthy older adults 60 years and older (Cansino,

2009), (2) native English speaker, (3) able to tolerate wearing an actigraphy, and (4) sufficient visual and auditory function for communication. The brief Michigan Alcoholism Screening Test-Revised (bMAST) and the Montreal Cognitive Assessment (MoCA) were used to screen the participants for eligibility. The exclusion criteria included (1) neurological disorders: Alzheimer's disease or other type of diagnosed dementia, neurodegenerative disorders (i.e., Parkinson's disease, Huntington's disease, and multiple sclerosis), traumatic brain injury with conscious loss > 30 minutes, epilepsy, stroke, the score of MoCA< 21, (2) active psychiatric problems based on DSM-V: major psychiatric disorders (i.e., bipolar disorder, schizophrenia, and major depression), substance abuse (i.e., illicit drug), the score of the bMAST ≥ 6, which identify alcoholism, and (3) chronic medical problems: heart failure, diagnosed sleep disorders, sleep apnea with continuous positive airway pressure therapy, end-stage renal disease with dialysis therapy, severe liver disease (i.e., liver cirrhosis and hepatic cancer), and current cancer with chemotherapy or radiotherapy. Persons with any of the above-mentioned exclusion criteria were not recruited for this research. Data on 62 eligible participants were collected during two home visits.

Procedures

Data collection was conducted by two face-to-face interviews a week apart at participants' homes or the University of Michigan, School of Nursing. During the first interview, the MoCA and bMAST were administrated to screen eligibility of potential participants after they signed inform consent to formally join this research. Demographic factor and healthy conditions were then collected from eligible participants and instruction of wearing actigraph device continuously for seven days was provided. After these 7 days of actigraphy measure, during the second interview, the actigraph device was taken back and self-reported sleep questionnaires (i.e., PSQI

and ESS) were administrated. The participants who completed data collection were given $20 give card as incentive and a brochure about healthy sleep.

Measures

Demographic factors and clinical conditions.

Participant demographic information (i.e., gender, age, race, year of education, marital status, occupation, employment status, weekly consumption of alcohol, caffeine intake, use of medications) was collected during face-to-face interviews at the first visit. Healthy conditions were determined by the Charlson Cormorbidity Index.

Screening tests.

Montreal Cognitive Assessment (MoCA).

The Montreal Cognitive Assessment (MoCA) was used to screen potential Alzheimer's disease or other type of diagnosed dementia by using a cut-off point of 21. The MoCA is a tool that screens for dementia by measuring global cognitive function. The components of the MoCA include the tasks of short-term memory recall, delayed memory recall, visuospatial/executive function, attention, language, abstraction, and orientation (Nasreddine et al., 2005).

Brief Michigan Alcohol Screening Test (bMAST).

The Brief Michigan Alcohol Screening Test (bMAST) was used to screen problematic alcoholism. The bMAST consists of 10 yes/no items. The possible scores range from 0 to 29. A higher total score indicates a higher possibility of problematic drinking behavior with a cutoff of 6 (Pokorny, Miller, & Kaplan, 1972). The reliability and construct validity of the bMAST have been established (Connor, Grier, Feeney, & Young, 2007).

Nighttime sleep disturbances.

Actigraphy.

Wrist actigraphy (ActiGraph, LLC. Pensacola, FL) was utilized to measure sleep disturbances objectively (Sadeh, Hauri, Kripke, & Lavie, 1995). For measuring sleep characteristics, the participants were required to wear the actigraph device on the non-dominant wrist continuously for seven nights so that body movement could be monitored and recorded to estimate sleep characteristics. The data recorded by the actigraph device were entered into ActiLife, the software provided by the device manufacturer (ActiGraph, Pensacola, FL) for analysis. The Cole-Kripke algorithm was used to calculate sleep characteristics including the total sleep duration, sleep latency, length and number of wakefulness after sleep onset (WASO), and length and number of long wakefulness after sleep onset (LWASO) (waking up after sleep onset while in bed > five minutes). A comparison of these data with the information participants reported in the sleep logs (time to bed and time to wake up) allowed total bed time and sleep efficiency to be determined. The validity of actigraphy for sleep measures has been well-established (R. J. Cole, Kripke, Gruen, Mullaney, & Gillin, 1992). The test-retest reliability of actigraghy performed in laboratory conditions was 0.98 which was adequate (Tryon, 2005). The sleep parameters for seven nights measured by an actigraph device was summed up and then divided by seven to obtain the means of sleep parameters, which were used for statistical analysis.

Sleep logs.

Participants maintained sleep logs to record the actual time that they went to bed and woke up each day during the seven days they wore the actigraph device. The duration between the two times is the total bed time. By comparing total bed time with the total sleep duration

obtained from the actigraphy, the sleep efficiency can be calculated. The numbers and length of daytime naps were recorded in the sleep logs.

Pittsburgh Sleep Quality Index (PSQI).

The Pittsburgh Sleep Quality Index (PSQI) which consists of 19 self-reported items was used to assess self-reported sleep disturbances. These self-reported items are categorized to seven subscales: 1) subjective sleep quality; 2) sleep latency; 3) sleep duration; 4) habitual sleep efficiency; 5) sleep disturbances; 6) use of sleep medications; and 7) daytime dysfunction. The total score ranges from 0 to 21. A higher score indicates poorer sleep quality with a cut-off point of five (Buysse et al., 1989). The validity and reliability of the PSQI have been well-established (Beaudreau et al., 2012; Cole et al., 2006)

Daytime sleepiness.

The Epworth Sleepiness Scale (ESS) was used to determine the level of daytime sleepiness in this study. The participants were asked to determine the likelihood of dozing off under the eight common statements. The responses of all statements are summed and the maximum score of the ESS is 24. A higher total score indicates more daytime sleepiness (Johns, 1991). The reliability and construct validity of the ESS are acceptable (Spira et al., 2012).

Depressive symptoms.

In this study, to evaluate depressive symptoms, the Geriatric Depression Scale-short form (GDS-S) was used which consists of 15 yes/no questions. Possible scores range from 0 to 15 and a higher total score indicates more depressive symptoms. The sensitivity and specificity of the GDS-S were determined. A total score higher than five suggests the presence of major depression (Wancata, Alexandrowicz, Marquart, Weiss, & Friedrich, 2006).

Statistical Analysis

IBM SPSS statistics (version 22, Armonk, NY) was used to analyze all the variables to fit the research purpose. Descriptive statistics were used to summarize demographic factors, clinical conditions, and all sleep parameters from actigraphy, the PSQI, the ESS, and sleep logs. To achieve aim 1, exploratory factor analysis was conducted to explore the factor structure and interrelationship among sleep parameters from actigraphy. The principal components method was used to extract factors; eigenvalues over Kaiser's criterion of >1 and a scree plot were used to determine factor numbers; the Varimax method was used to rotate factor loading (Polit, 2010). The factor scores of the sleep parameters from actigraphy were created by regression method for analysis of aim 2.

To achieve aim 2, Pearson's correlation and hierarchical multiple regression were conducted to explore the association between sleep parameters from the self-reported questionnaires (i.e., PSQI and ESS) and the factor score of sleep parameters from actigraphy after controlling related factors (i.e., gender, depressive symptoms, health conditions). In the regression models, three sleep factor scores obtained from actigraphy were entered as dependent variables individually. Self-reported sleep parameters [i.e., self-reported sleep latency, self-reported sleep duration, self-reported sleep efficiency from the PSQI, total PSQI score (sleep quality), total ESS score (daytime sleepiness), daytime naps from sleep logs] were entered as independent variables simultaneously. Gender, depressive symptoms, and health conditions were entered as covariates. P value <.05 was used to determine significance (Polit, 2010).

Results

Sample Characteristics

A convenience sample of 62 healthy older adults was enrolled into this study. Table 3.2, presents the characteristics of this sample. Among this sample, 75% were female; racial distribution was predominantly White (87%); and 90% had bachelor's degree or higher. For substance consumption, no one currently smoked nicotine cigarettes and 21% did not drink any alcohol during the past 30 days. The evaluation of healthy conditions showed that one third of participants had hypertension or hyperlipidemia and only six of the participants took over-the-counter medications [melatonin or diphenhydramine (BENADRYL ®)] for sleep.

Sleep Parameters

All participants completed the two self-reported questionnaires, the PSQI and the ESS. Fifty-six (90 %) of them completed 7-night actigraphic sleep assessment and sleep logs; 5 (8%) wore the actigraphy for only 6 nights; and one (2%) wore this device for only 5 nights. The means of the sleep parameters from the nightly actigraphy were used for analysis. The results of the statistical analysis of sleep parameters obtained from the PSQI, the ESS, actigraphy, and the sleep logs are shown in Table 2. The results of the PSQI showed that 44% had total PSQI score > 5, indicating poor sleep quality and the results of the ESS showed that only 8 % had total ESS score > 10, indicating excessive daytime sleepiness. The results of the sleep logs showed that 50% had never taken any naps during the day over the course of data collection.

Exploratory factor analysis was conducted to determine the factor structure of the different sleep parameters recorded via actigraphy. The results showed that these sleep parameters fit a Varimax-rotation three-factor solution, which explained 86% of scale variance of actigraphy with the item loading ranging from 0.52 to 0.96 (See Table 3.3). Five sleep

parameters, sleep efficiency, the total length of WASO, the average length of each WASO, the numbers of LWASO, and the average length of each LWASO loaded on factor 1, which was labeled wakefulness during sleep periods (eigenvalue of 3.7). Two sleep parameters sleep latency and the numbers of WASO loaded on factor 2, which was labeled difficulty in falling and staying asleep (eigenvalue of 2.2). The remaining two sleep parameters, total bed time and total sleep duration loaded on factor 3, which was labeled sleep time (eigenvalue of 1.9). The value of the Kaiser-Meyer-Olkin Measure test was 0.55, and the result of the Barlett's Test of Sphericity was significant ($p<.001$), indicating an acceptable sample adequacy. The factor scores were created by regression method for analysis.

Association between Self-Reported and Objective Sleep Parameters

Table 3.4, presents the results of Pearson's correlation to determine the relationship between self-reported sleep parameters and sleep factors obtained from actigraphy. The results showed that objective wakefulness during sleep periods (factor 1) was significantly correlated with self-reported sleep duration ($r=-0.27$, $p<.05$), sleep efficiency ($r= -0.46$, $p<.01$), and sleep quality ($r=0.35$, $p<.01$) from the PSQI but these correlations were low to moderate. The decrease in self-reported sleep efficiency and sleep duration were correlated with an increase in objective wakefulness during sleep periods in older adults. Poor sleep quality was related to an increase in objective wakefulness (factor 1) in this population. Objective sleep time (factor 3) was significantly and strongly correlated with self-reported sleep duration ($r= 0.51$, $p<.01$) and low with daytime naps ($r=-0.27$, $p<.05$). An increase in self-reported sleep duration was associated with an increase in objective sleep time, while increase in daytime naps was correlated with decrease in objective sleep time (factor 3) in older adults. Objective difficulty in falling and staying asleep (factor 2) was not significantly correlated with any self-reported sleep parameters.

This result suggests that objective sleep difficulties for falling and staying asleep (factor 2) was not related to self-reported sleep parameters in healthy older adults.

Pearson's correlation indicated that healthy conditions were significantly and moderately correlated with daytime naps ($r=0.42$, $p<.01$). Depressive symptoms were significantly correlated with self-reported sleep efficiency ($r=-0.26$, $p<.05$) and sleep quality ($r=0.31$, $p<.05$) but magnitude of the correlation was low.

The results of all multiple regression models testing the hypotheses are shown in Table 3.5. In the first model, self-reported sleep parameters [i.e., self-reported sleep latency, self-reported sleep duration, self-reported sleep efficiency from the PSQI, total PSQI score (sleep quality), total ESS score (daytime sleepiness), daytime naps from sleep logs] were entered as independent variables and objective wakefulness during sleep periods (factor 1) was entered as a dependent variable. The results showed that after controlling for the covariates (i.e., gender, depressive symptoms, and health conditions), this model significantly explained objective wakefulness during sleep periods (factor 1) [Overall $R^2 = .27$, Adjusted $R^2 = .14$, $\Delta R^2 = 0.23$, $F(9, 52) = 2.13$, $p=.043$]. Only self-reported sleep efficiency from the PSQI was an independent predictor of objective wakefulness during sleep periods (factor 1) ($\beta = -0.50$, $p=.021$). These results indicate that a lower self-reported sleep efficiency explained more objective wakefulness during sleep periods in this sample of older adults after controlling for the influence of gender, depressive symptoms, and healthy conditions.

In regression model 2, self-reported sleep parameters were entered as independent variables and objective difficulty in falling and staying asleep (factor 2) was entered as a dependent variable. The results showed that after controlling covariates (i.e., gender, depressive symptoms, and health conditions), this model cannot significantly explain objective difficulty in

falling and staying asleep (factor 2) [Overall R^2 = .20, Adjusted R^2 = .06, Δ R^2= 0.14, F (9, 52) = 1.41, p=.210].

In regression model 3, self-reported sleep parameters were entered as independent variables and objective sleep time (factor 3) was entered as a dependent variable. The results showed that after controlling covariates (i.e., gender, depressive symptoms, and health conditions), this model significantly explained objective sleep time [Overall R^2 = .69, Adjusted R^2 = .63, Δ R^2= .64, F (9, 52)= 12.56, p=.000]. Self-reported sleep duration (β= 1.08, p=.000) and sleep efficiency from the PSQI (β= -0.65, p=.000) were significant predictors of objective sleep time (factor 3), indicating that among healthy older adults, a longer objective sleep time was substantially explained by a longer self-reported sleep duration and lower self-reported sleep efficiency after excluding the influence of related factors.

Discussion

In this descriptive study, increased objective wakefulness during sleep periods was correlated with decreased self-reported sleep duration, decreased sleep efficiency, and poorer sleep quality. Increased objective sleep time was correlated with decreased daytime naps. Although these correlations were significant, the magnitude was low to medium. The results of hierarchical multiple regression indicated that that self-reported sleep parameters [i.e., self-reported sleep latency, self-reported sleep duration, self-reported sleep efficiency from the PSQI, the total PSQI score (sleep quality), the total ESS score (daytime sleepiness), daytime naps from sleep logs] significantly explained objective wakefulness during sleep periods (R^2= 0.23, p=.043) and sleep time (R^2= 0.64, p<.001), after controlling for gender, depressive symptoms, and healthy conditions.

Self-reported sleep efficiency was a significant predictor of objective wakefulness during sleep periods (β =-0.50, p<.05). A higher self-reported sleep efficiency explained less objective wakefulness during sleep period. Self-reported sleep duration ($\beta = 1.08, p < .001$) and sleep efficiency ($\beta = -0.65, p < .001$) were significant predictors of objective sleep time. A longer self-reported sleep duration explained a longer objective sleep time; however, unexpectedly, a lower self-reported sleep efficiency explained a longer objective sleep time. These results are partially consistent with the results from Vitiello et al. (2004) and McCrae et al. (2005), each of which reported a significant correlation between self-reported and objectively measured sleep duration (McCrae et al., 2005; Vitiello et al., 2004). The possible explanation for this unexpected result may be that older adults who thought they needed more time to fall asleep (overestimated sleep latency) tended to go to bed earlier and to stay in bed longer (longer total bed time), leading to reduced self-reported sleep efficiency. Objective sleep time as recorded by actigraphy included total bed time and total sleep duration which contributed a negative correlation with self-reported sleep efficiency and objective sleep time as recorded by actigraphy. Thus, reduced self-sleep efficiency explained longer objective sleep time as recorded by actigraphy. This finding still needs further confirmation.

These results contribute the body of knowledge regarding sleep disturbances in older adults. First, objective sleep time was significantly and substantially explained by self-reported sleep parameters (64% of variance), the correlation between self-reported and objectively measured sleep time was strong and significant (r= 0.51, p<.01). Self-reported and actigraphic measured total sleep duration were similar (6.85 hours and 6.96 hours, respectively). The studies by Vitiello and colleagues (2004) and Rotenberg et al. (2000) indicated that self-reported sleep duration had significant, but low to moderate, correlations with objective sleep time from the

polysomnography and actigraphy (Rotenberg et al., 2000; Vitiello et al., 2004) and that only around 25% of individuals can correctly estimate their sleep duration (Rotenberg et al., 2000). Compared to the above-mentioned two studies, the results of the current study demonstrated a stronger relationship between self-reported sleep parameters and objective sleep time after controlling for the influence of gender, depressive symptoms, and healthy conditions. This suggests that after controlling for the influence of covariates, objective sleep time and self-reported sleep parameters are not as different as has been previously reported.

Another contribution of this study is the finding of the differences between objective wakefulness during sleep periods and difficulty in falling and staying asleep in terms of self-reported sleep parameters. The results of Pearson's correlation revealed that more objective wakefulness during sleep periods as measured by actigraphy was correlated with shorter self-reported sleep duration ($r=-0.27$, $p<.05$), lower sleep efficiency ($r= -0.46$, $p<.01$) and poorer sleep quality ($r=0.35$, $p<.01$) but these correlation were small to medium. These results are consistent with Hart et al. (1995), who found weak correlations between sleep latency and sleep efficiency, as reported in a sleep diary and as recorded via the polysomnography (Hart et al., 1995). The results of hierarchical multiple regression found that although objective wakefulness during sleep periods as measured by actigraphy was significantly explained by self-reported sleep parameters, the explained variance was only 23% to 24%. The objective difficulty in falling and staying asleep was more independent from self-reported sleep parameters. After controlling for the influence of the covariates (i.e., gender, depression, and healthy conditions), objective wakefulness during sleep periods and difficulty in falling and staying asleep accounted for more unmeasured variables such as cognitive dysfunction and functional disability with aging. Thus, it is hard to fully explain the finding related to objective wakefulness during sleep periods

and difficulties falling and staying asleep on the basis of self-reported sleep parameters. These results are consistent with Rotenberg et al. (2000) who found that only 10% of healthy older adults can correctly estimate sleep fragmentation and 30% can correctly estimate sleep latency (Rotenberg et al., 2000), indicating difficulties to obtain correct sleep assessments only from self-reported sleep questionnaires and implying substantial differences between self-reported sleep parameters and objective wakefulness during sleep periods and difficulties falling asleep and staying sleep.

The sleep parameters as recorded via actigraphy were analyzed by exploratory factor analysis to determine their factor structure. The results revealed a three-factor solution that explained approximately 86% of scale variance with an acceptable sample adequacy. These three sleep factors demonstrated three important sleep disturbances domains of older adults: 1) wakefulness during sleep periods, 2) difficulty in falling and staying asleep, and 3) sleep time. These sleep disturbances domains are consistent with the characteristics of sleep disturbances of older adults found in previous studies such as difficulties falling asleep or staying asleep, increased sleep latency, increased long fragmented sleep, decreased total sleep duration, and decreased sleep efficiency (Blackwell et al., 2011; Edwards et al., 2010; Ensrud et al., 2009; Espiritu, 2008).

Some previous studies have found that gender (McCrae et al., 2005; Vitiello et al., 2004), depressive symptoms (Rotenberg et al., 2000), and health conditions (McCrae et al., 2005) could influence how well individuals estimate their sleep and further affects the identification of the relationship between self-reported and objective sleep. In this study, the results of Pearson's correlation showed that more daytime sleepiness was related to poorer health conditions and lower self-reported sleep efficiency. Moreover, poor sleep quality was related to increased

depressive symptoms. No actigraphic measured sleep factors were significantly related to health conditions and depressive symptoms, suggesting that the use of actigraphy to measure sleep is not such influenced by other factors and relate, possibly, to different domains of sleep. The results of hierarchical multiple regression analysis demonstrated that only daytime naps were explained by health conditions. Gender and depressive symptoms did not explain sleep disturbances in older adults in this study.

Overall, only measures of sleep duration from self-reported questionnaires and as recorded by actigraphy were substantially correlated to each other. Although objective wakefulness during sleep periods as recorded via actigraphy was significantly explained by self-reported sleep parameters after controlling for the effect of related factors, this association was weak. Objective difficulty in falling and staying asleep was independent from self-reported sleep parameters. These results suggest that there are significant differences between these two types of measures and a potential for unmeasured factors to influence the relationship between self-reported and objective measured sleep. The sleep fragmentation, difficulty in falling asleep or maintaining sleep, reduced sleep efficiency, daytime sleepiness, poor sleep quality which are observed symptoms of age-related sleep disturbances (Blackwell et al., 2011; Edwards et al., 2010; Ensrud et al., 2009; Espiritu, 2008), were difficult to assess by a single measure. These results suggest that the utilization of sleep measures in research requires the consideration of the research purpose or sample characteristics in future studies. For instance, the study focus on wakefulness during sleep periods may need objective sleep measure to obtain completed information of this sleep variable. Further investigations are needed to understand the association and differences between self-reported and objective sleep in older adults.

This study has several limitations. The first is due to selection bias in sample recruitment. Potential bias include: most of participants were recruited from one geographic area; educational years (18.17 years) was higher than mean educational years of adults in the U.S. (12.9 years in 2013) (United Nations, 2013); the majority of this sample (75.8%) was female; and the racial distribution was predominantly white (87.1%). The second limitation is lack of longitudinal measures of sleep over extended periods of time in this study. This was a cross-sectional study. Actigraphic data were derived from means of 7-night data, which is substantial, but this was done only on a period of seven consecutive days. The lack of longitudinal measures creates difficulties in determining changes in sleep over time among older adults. Future studies should include objective measures of daytime sleepiness, recruit a more diverse sample, and measure changes of sleep over longer time. The strength of this study is that to our knowledge, this study was one of the first study to investigate the factor structure of sleep parameters as recorded via actigraphy. This study may be the first to investigate the relationship between self-reported and objectively measure sleep parameters after controlling for the influence of related factors such as gender, healthy conditions, and depression.

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Table 3.1
The Characteristics of Sleep Disturbances of Older Adults

	Sleep characteristics
Self-reported	Difficulty in falling asleep or maintaining sleep
	Increased long fragmented sleep (wakefulness after sleep onset> five minutes)
	More daytime sleepiness
	Early morning awakening
	Decreased total sleep duration (total hours of sleep while in bed)
	Decreased sleep efficiency (percentage of total sleep duration while in the bed)
	Increased sleep latency (amount of time until sleep onset while in bed)
	Increased number and length of daytime napping
	Poor sleep quality
Objectively measured	Reduction of total sleep duration (around 10 minute per decade)
	Decreased sleep efficiency
	Decreased stage three and four of NREM sleep, which is SWS (2% per decade from the age of 60)
	Decreased REM sleep (from the age of 60)
	Decreased number of sleep cycles per night
	Increased sleep latency
	Increased stage one and two of NREM sleep
	Increased number of long fragmented sleep episodes (waking up after sleep onset while in bed > five minutes)

Note. NREM= non-rapid eye movement; SWS= slow wave sleep; REM=rapid eye movement.

Table 3.2.

Descriptive Statistics for Sample Characteristics and Sleep Parameters (N=62; male/female= 17/47)

Variables	N (%)	Mean (SD)	Median	Range
Age (years)		69.9 (7.1)	68.50	60-88
Educational years		18.2 (3.1)	18.00	12-28
Educational level				
High school	4 (6.5)			
Trade school or associate degree	2 (3.2)			
Bachelor	25 (40.3)			
Master	20 (32.3)			
Doctoral	11 (17.7)			
Race				
White	54 (87.1)			
African American	6 (9.7)			
Asian	1 (1.6)			
More than one race	1(1.6)			
Smoking history (pack years)		25.3 (34.5)	7.50	0.0-140
Days drinking alcohol / 30 days		7.2 (8.6)	3.75	0-30
Coffee / day (cups=8 oz.)		1.6 (1.7)	1.50	0.0-7.0

(continued)

Table 3.2 (continued)

Variables	N (%)	Mean (SD)	Median	Range
Tea / day (cup=8oz.)		0.8 (1.1)	0.18	0.0-5.5
Cola /day (cup=8oz.)		0.4 (1.0)	0.00	0.0-6.0
Charlson Comorbidity Index		0.4 (0.7)	0.00	0.0-3.0
Geriatric Depression Scale		1.2 (2.1)	0.0	0.0-14.0
Sleep Disturbances				
PSQI				
Sleep duration (hours)		6.9 (1.0)	7.00	4.5-9.0
Sleep latency (minutes)		18.3 (16.6)	15.00	2.5-90.0
Sleep efficiency (%)		87.0 (9.4)	87.50	50.0-100.0
Total score		5.2 (2.9)	5.00	1.0-14.0
Total score of ESS		5.3 (3.2)	5.00	0.0-13.0
Actigraphy				
Sleep latency (minutes)		3.5 (4.0)	2.79	0.0-26.4
Sleep efficiency (%)		89.6 (5.0)	90.80	72.2-96.3
Total bed time (hours)		7.8 (0.9)	7.83	5.8-9.5
Total sleep duration (hours)		7.0 (0.8)	6.90	5.0-8.8
Total length of WASO (minutes)		45.8 (24.9)	40.86	15.0-134.8
Numbers of WASO		12.5 (4.4)	11.86	5.4-23.7

(continued)

Table 3.2 (continued)

Variables	N (%)	Mean (SD)	Median	Range
Average length of each WASO (minutes)		3.6 (1.1)	3.31	2.0-7.0
Numbers of long WASO (WASO>5 min) (minutes)		3.2 (1.8)	2.71	0.7-9.3
Average length of each long WASO (WASO>5 min) (minutes)		9.0(2.1)	8.77	5.1-15.7
Sleep logs: length of naps /day (minutes)		4.8 (12.9)	0.41	0.0-89.4

Note, PSQI= Pittsburgh Sleep Quality Index; ESS=Epworth Sleepiness Scale; WASO= Wakefulness after sleep onset

Table 3.3.

Factor Analysis of Actigraphic Sleep Measured Results (n=62)

Objective sleep parameters	Rotated Factor Loadings			Communality
	1	2	3	(h^2)
Sleep latency (minutes)	-.06	**.52**	-.03	.271
Sleep efficiency (%)	**-.75**	-.64	.11	.992
Total bed time (hours)	.21	.20	**.96**	.997
Total sleep duration (hours)	-.18	-.13	**.97**	.997
Total duration of WASO (minutes)	**.79**	.58	.09	.968
The numbers of WASO	.28	**.88**	.14	.864
The average duration of WASO (minutes)	**.96**	-.05	.01	.930
The numbers of long WASO (WASO>5 min)	**.76**	.58	.08	.915
The average duration of long WASO (WASO>5 min) (minutes)	**.90**	-.00	-.00	.814
Eigenvalue	3.66	2.18	1.91	7.75
Percent of Variance Explained	40.67	24.19	21.22	86.08%

NOTE: Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization, All loadings greater than .40 are in bold. WASO= Wakefulness after sleep onset

Table 3.4

Pearson's Correlations between Self-reported Sleep Parameters and Sleep Factors Obtained from Actigraphy (n=62)

Variables	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
1. Factor 1: wakefulness during sleep periods								
2. Factor 2: difficulty in falling and staying asleep	.00							
3. Factor 3: sleep time	.00	.00						
4. PSQI_sleep latency	.20	.24	.13					
5. PSQI_sleep duration	-.27*	.03	.51**	-.45**				
6. PSQI_sleep efficiency	-.46**	-.15	-.10	-.60**	.67**			
7. PSQI_Total score (sleep quality)	.35**	.07	.03	.62**	-.63**	-.76**		
8. ESS_Total score (daytime sleepiness)	-.03	-.01	-.06	.08	-.07	-.13	.23	
9. Daytime naps	-.01	-.15	-.27*	-.05	-.16	-.12	.13	.22

Note, PSQI= Pittsburgh Sleep Quality Index; ESS=Epworth Sleepiness Scale

*p<.05 **p<.01

Table 3.5

Multiple Regression Predicting Factor Scores of Sleep Parameters from Actigraphy (n=62)

Predictors	**Factor scores of Sleep Parameters from Actigraphy**					
	Wakefulness during sleep periods (Model 1)		**Difficulties for falling and staying asleep(Model 2)**		**Sleep time (Model 3)**	
	Step 1	**Step 2**	**Step 1**	**Step 2**	**Step 1**	**Step 2**
	β		***β***		***β***	
Gender	.10	.09	-.26	-.32	.11	-.02
Depressive symptoms (GDS_Total score)	.01	-.14	-.05	-.15	.24	.06
Health conditions (Charlson comorbidity index)	.21	.22	-.08	-.07	-.12	-.12
PSQI_Self-reported sleep latency		-.17		.28		.12
PSQI_Self-reported sleep duration		.06		.27		1.08***
PSQI_Self-reported sleep efficiency		-.50*		-.34		-.65***
PSQI_Total score (sleep quality)		.17		-.19		.18
ESS_Total score (daytime sleepiness)		-.09		.02		-.10
Sleep logs_daytime naps		-.15		-.12		-.13
R^2	.02	.27	.05	.20	.05	.69
Adjusted R^2	-.01	.14	.00	.06	-.00	.63
ΔR^2		.23		.14		.64
Overall Sig.	.511	.043	.363	.210	.422	.000

*p<.05, **p<.01, ***p<.001

References

Beaudreau, S. A., Spira, A. P., Stewart, A., Kezirian, E. J., Lui, L. Y., Ensrud, K., . . . Stone, K. L. (2012). Validation of the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale in older black and white women. *Sleep Medicine, 13*(1), 36-42. doi: 10.1016/j.sleep.2011.04.005

Blackwell, T., Yaffe, K., Ancoli-Israel, S., Redline, S., Ensrud, K. E., Stefanick, M. L., . . . Stone, K. L. (2011). Association of sleep characteristics and cognition in older community-dwelling men: the MrOS sleep study. *Sleep, 34*(10), 1347-1356. doi: 10.5665/sleep.1276

Buysse, D. J., Reynolds, C. F., 3rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research, 28*(2), 193-213.

Cansino, S. (2009). Episodic memory decay along the adult lifespan: a review of behavioral and neurophysiological evidence. *International Journal of Psychophysiology, 71*(1), 64-69. doi: 10.1016/j.ijpsycho.2008.07.005

Cole, J. C., Motivala, S. J., Buysse, D. J., Oxman, M. N., Levin, M. J., & Irwin, M. R. (2006). Validation of a 3-factor scoring model for the Pittsburgh sleep quality index in older adults. *Sleep, 29*(1), 112-116.

Cole, R. J., Kripke, D. F., Gruen, W., Mullaney, D. J., & Gillin, J. C. (1992). Automatic sleep/wake identification from wrist activity. *Sleep, 15*(5), 461-469.

Connor, J. P., Grier, M., Feeney, G. F., & Young, R. M. (2007). The validity of the Brief Michigan Alcohol Screening Test (bMAST) as a problem drinking severity measure. *Journal of Studies on Alcohol and Drugs, 68*(5), 771-779.

Edwards, B. A., O'Driscoll, D. M., Ali, A., Jordan, A. S., Trinder, J., & Malhotra, A. (2010). Aging and sleep: physiology and pathophysiology. *Seminars in Respiratory and Critical Care Medicine, 31*(5), 618-633. doi: 10.1055/s-0030-1265902

Ensrud, K. E., Blackwell, T. L., Redline, S., Ancoli-Israel, S., Paudel, M. L., Cawthon, P. M., . . . Osteoporotic Fractures in Men Study, G. (2009). Sleep disturbances and frailty status in older community-dwelling men. *Journal of the American Geriatrics Society, 57*(11), 2085-2093. doi: 10.1111/j.1532-5415.2009.02490.x

Espiritu, J. R. (2008). Aging-related sleep changes. *Clinics in Geriatric Medicine, 24*(1), 1-14, v. doi: 10.1016/j.cger.2007.08.007

Foley, D. J., Monjan, A. A., Brown, S. L., Simonsick, E. M., Wallace, R. B., & Blazer, D. G. (1995). Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep, 18*(6), 425-432.

Grimes, D. A., & Schulz, K. F. (2002). An overview of clinical research: the lay of the land. *Lancet, 359*(9300), 57-61. doi: 10.1016/s0140-6736(02)07283-5

Hart, R. P., Morin, C. M., & Best, A. M. (1995). Neuropsychological performance in elderly insomnia patients. *Aging, Neuropsychology, and Cognition, 2*(4), 268-278.

Johns, M. W. (1991). A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep, 14*(6), 540-545.

McCrae, C. S., Rowe, M. A., Tierney, C. G., Dautovich, N. D., Definis, A. L., & McNamara, J. P. (2005). Sleep complaints, subjective and objective sleep patterns, health, psychological adjustment, and daytime functioning in community-dwelling older adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 60*(4), P182-189.

Nasreddine, Z. S., Phillips, N. A., Bedirian, V., Charbonneau, S., Whitehead, V., Collin, I., . . . Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society, 53*(4), 695-699. doi: 10.1111/j.1532-5415.2005.53221.x

Pokorny, A. D., Miller, B. A., & Kaplan, H. B. (1972). The brief MAST: a shortened version of the Michigan Alcoholism Screening Test. *The American Journal of Psychiatry, 129*(3), 342-345.

Polit, D. F. (2010). *Statistics and Data Analysis for Nyrsing Research*. Upper Saddle River, NJ: Pearson Education Inc.

Rotenberg, V. S., Indursky, P., Kayumov, L., Sirota, P., & Melamed, Y. (2000). The relationship between subjective sleep estimation and objective sleep variables in depressed patients. *International Journal of Psychophysiology, 37*(3), 291-297.

Sadeh, A., Hauri, P. J., Kripke, D. F., & Lavie, P. (1995). The role of actigraphy in the evaluation of sleep disorders. *Sleep, 18*(4), 288-302.

Spira, A. P., Beaudreau, S. A., Stone, K. L., Kezirian, E. J., Lui, L. Y., Redline, S., . . . Osteoporotic Fractures in Men, S. (2012). Reliability and validity of the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale in older men. *The Journals of Gerontology.Series A, Biological Sciences and Medical Sciences, 67*(4), 433-439. doi: 10.1093/gerona/glr172

Tryon, W. W. (2005). The reliability and validity of two ambulatory monitoring actipraphs. *Behavior Research Methods, 37*(3), 492-497.

United Nations (2013), United nations development programe:Human Development Reports. 09 April 2015. Retrieved from http://hdr.undp.org/en/content/mean-years-schooling-adults-years

Vitiello, M. V., Larsen, L. H., & Moe, K. E. (2004). Age-related sleep change: Gender and estrogen effects on the subjective-objective sleep quality relationships of healthy, noncomplaining older men and women. *Journal of Psychosomatic Research, 56*(5), 503-510. doi: 10.1016/s0022-3999(04)00023-6

Wancata, J., Alexandrowicz, R., Marquart, B., Weiss, M., & Friedrich, F. (2006). The criterion validity of the Geriatric Depression Scale: a systematic review. *AJournal of Psychosomatic Research, 114*(6), 398-410. doi: 10.1111/j.1600-0447.2006.00888.x

Chapter Four

The Relationship between Sleep Disturbances and Episodic Memory among Older Adults

Abstract

Objective: The purposes of this study were to examine the relationship between sleep disturbances and episodic memory performance in older adults and to analyze the role of attention, executive function, cognitive reserve, depressive symptoms, and aging in the relationship between sleep disturbances and episodic memory.

Methods: In this cross-sectional descriptive study, a convenience sample was recruited from the Michigan Alzheimer's Disease Center and the database of Clinical Study of University of Michigan. The sample size was 62 older adults age 60 and older. Two self-reported questionnaires and actigraphy were used to measure sleep and the Hopkins Verbal Learning Test-Revised was used to measure episodic memory. Descriptive statistics, Pearson's correlation, exploratory factor analysis, and hierarchical multiple regression analyses were conducted to achieve study aim.

Results: In older adults, sleep disturbances as measured by self-reported questionnaires and actigraphy, age, depressive symptoms, attention, executive function, and cognitive reserve explained episodic memory performance (i.e., delayed recall and learning effect) after controlling for the influence of covariates (i.e., gender, educational years, BMI, and healthy conditions). Daytime sleepiness, difficulty in falling asleep and maintaining sleep, executive function, and cognitive reserve were significant predictors of diminished episodic memory. Depressive symptoms were a significant moderator between sleep disturbances and episodic

memory in older adults. Compared to the older adults with fewer depressive symptoms, the influence of sleep disturbances in episodic memory was stronger among those with more depressive symptoms.

Discussion: These results point to interesting directions for future sleep intervention studies that are designed to improve episodic memory in older adults. To continue to deepen understanding of the relationship between sleep and episodic memory, studies may need to include more biological variables such as genotype, inflammatory biomarkers, and physical activity. In the current study, depressive symptoms influenced the relationship between sleep disturbances and episodic memory. Thus, in future studies that investigate sleep and episodic memory in older adults, depressive symptoms need to be measured.

Introduction

Episodic memory is a subtype of declarative or explicit memory that is involved in the learning, storage, and retrieval of personal experiences and personal meaning (Dickerson & Eichenbaum, 2010). Episodic memory is essential for an individual's ability to construct the world and the concept of self (Squire & Kandel, 2009). In addition to this function, episodic memory is involved in early semantic learning (Merritt et al., 2006) and skill learning (Beaunieux et al., 2009). Importantly, episodic memory is associated with functional ability [i.e., activities of daily living (ADLs) and instrumental activities of daily living (IADLs)] (Burton et al., 2006; Goldberg et al., 2010; Tomaszewski Farias et al., 2009a) and mortality in older adults (Lavery et al., 2009; Lee et al., 2006). When episodic memory is impaired, functional ability is decreased while mortality is increased in older adults with (Lee et al., 2006) and without dementia (Lavery et al., 2009). Given the importance of episodic memory in daily life, it is important to investigate the factors that may contribute to impaired episodic memory.

Episodic memory can become impaired in response to a variety of factors including, age, depressive symptoms, and sleep disturbances. Sleep disturbances are a common problem for many older adults, with around 50% of older adults complaining about chronic sleep disturbances (Foley et al., 1995) and poor sleep quality (Blackwell et al., 2011; Martin et al., 2010). The most common characteristics of sleep disturbances in older adults are presented in Table 4.1.

Table 4.1

The Characteristics of Sleep Disturbances among Older Adults

	Sleep characteristics
Self-reported	Difficulty in falling asleep or maintaining sleep
	Increased long fragmented sleep (wakefulness after sleep onset> five minutes)
	More daytime sleepiness
	Early morning awakening
	Decreased total sleep duration (total hours of sleep while in bed)
	Decreased sleep efficiency (percentage of total sleep duration while in the bed)
	Increased sleep latency (amount of time until sleep onset while in bed)
	Increased number and length of daytime napping
	Poor sleep quality
Objectively measured	Reduction of total sleep duration (around 10 minute per decade)
	Decreased sleep efficiency
	Decreased stage three and four of NREM sleep, which is SWS (2% per decade from the age of 60)
	Decreased REM sleep (from the age of 60)
	Decreased number of sleep cycles per night
	Increased sleep latency
	Increased stage one and two of NREM sleep
	Increased number of long fragmented sleep episodes (waking up after sleep onset while in bed > five minutes)

Note. NREM= non-rapid eye movement; SWS= slow wave sleep; REM=rapid eye movement.

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Sleep consists of two stages: rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep, both of which are necessary for episodic memory consolidation (Poe et al., 2010; Rauchs et al., 2005). Studies have shown that during sleep, there is a co-activation of the hippocampus and the neocortical areas and changes in neurotransmitters (Rauchs et al., 2005) and after sleep, older adults have been found to perform better on episodic memory tests (Aly & Moscovitch, 2010; Fenn et al., 2009; Hornung et al., 2007; Wilson et al., 2012). Alternatively, the artificial restriction or deprivation of sleep [e.g. total sleep duration, REM sleep deprivation, stage 2 NREM sleep deprivation, slow wave sleep disruption (SWS)] are known to cause a decline in episodic memory performance (Backhaus et al., 2007; Stenuit & Kerkhofs, 2008; Van Der Werf et al., 2011).

Studies of older adults have shown that self-reported sleep disturbances were negatively correlated with performance on episodic memory tests (Bonanni et al., 2005; Ferrie et al., 2011; Haimov, 2006; Kronholm et al., 2009; Loerbroks et al., 2010; Nebes et al., 2009; Ohayon & Vecchierini, 2002; Schmutte et al., 2007; Sutter et al., 2012; Tworoger et al., 2006; Westerberg et al., 2010; Xu et al., 2011). Self-reported sleep duration shows a reversed U-shape association with episodic memory performance. Specifically, older adults with 6 to 8 hours of sleep had better episodic memory than older adults with either ≤ 5 hours or ≥ 9 hours of sleep (Ferrie et al., 2011; Kronholm et al., 2009; Loerbroks et al., 2010; Schmutte et al., 2007; Tworoger et al., 2006; Xu et al., 2011). In addition to self-reported sleep duration, other self-reported sleep disturbances [i.e., daytimes sleepiness, increased daytime napping (Bonanni et al., 2005; Ohayon & Vecchierini, 2002), and difficulty in falling asleep and maintaining sleep (Tworoger et al., 2006; Westerberg et al., 2010)] have been correlated with poorer episodic memory in older adults. Although it is known that self-reported sleep disturbances are associated with poorer episodic

memory, which characteristics of self-reported sleep disturbances more strongly correlate with episodic memory and whether self-reported sleep disturbances can explain episodic memory among older adults remains to be fully determined.

Objectively measured sleep characteristics [i.e., sleep duration (Cochrane et al., 2012; Westerberg et al., 2010; Hart et al., 1995), proportion of sleep cycle (Mazzoni et al., 1999), total bed time (Westerberg et al., 2010), sleep fragmentation (Westerberg et al., 2010), duration of SWS (Backhaus et al., 2007)] have been shown to be significantly correlated with episodic memory among older adults (Backhaus et al., 2007; Cochrane et al., 2012; Hart et al., 1995; Mazzoni et al., 1999; Oosterman et al., 2009; Westerberg et al., 2010). For instance, a study by Hart et al. (1995) (n=78) indicated that objective total sleep duration can explain episodic memory in healthy older adults (R^2=0.13, p<.01) (Hart et al., 1995), but the direction of this association was unclear. Another two studies by Westerberg et al. (2010) (n=20) and Cochrane et al. (2012) (n=26) found that objective total sleep duration (Westerberg et al., 2010; Cochrane et al., 2012), sleep latency and sleep fragmentation (Westerberg et al., 2010) were negatively associated with episodic memory in healthy older adults and the patients with cognitive impairment. However, the sample size of this study was less than 30 and included both healthy older adults and the patients with cognitive impairment, making it difficult to generalize the influence of sleep disturbances on episodic memory to the broader elderly population.

In addition to sleep disturbances, aging (Rosenzweig & Barnes, 2003) and depressive symptoms (Beaudreau & O'Hara, 2009; Gonzalez et al., 2008; Panza et al., 2009) have been associated with episodic memory decline. The decline in episodic memory may start as early as age 31 (Cansino, 2009). This decline in episodic memory can manifest itself as a failure to differentiate re-experienced memory and newly encoded information, particularly spatial

information, and the dysfunction of episodic memory retrieval (Dickerson & Eichenbaum, 2010). The link between depression and episodic memory may be attributable to hippocampal atrophy, which is the most important brain region for episodic memory (Fotuhi et al., 2012). Depressive symptoms have been significantly correlated with deficits of episodic memory (Beaudreau & O'Hara, 2009; Gonzalez et al., 2008; Panza et al., 2009).

In addition to episodic memory, sleep disturbances may influence other cognitive functions (i.e., attention, executive function, and cognitive reserve) and are correlated with depressive symptoms that simultaneously affect episodic memory. Older adults with self-reported daytime sleepiness, shorter sleep time ≤ 5 hours, and taking sleep medicine had more impaired attention than the group without these sleep problems (Ohayon & Vecchierini, 2002). Alternatively, older adults with good sleep quality (Nebes et al., 2009; Sutter et al., 2012) and short sleep latency (Schmutte et al., 2007) were found to have better attention. However, increased odds of attention declines associated with higher level of objectively measured wakefulness after sleep onset, long wake episodes, and lower sleep efficiency (Blackwell et al., 2014). The declines of attention are important because it may contribute to episodic memory deficits and affect the formation of episodic memory (Cole & Richards, 2005).

In addition to its association with attention, sleep, particularly slow wave sleep (SWS), is associated with executive function and function of the prefrontal cortex, the primary brain region that supports executive function. Studies have shown that total sleep deprivation is associated with dysfunction of the prefrontal cortex and deficits of executive function (Harrison & Horne, 1999; Harrison et al., 2000). Poor executive function in older adults has been associated with fragmentation of sleep-wake rhythm (Oosterman et al., 2009) and sleep onset/maintenance difficulties (Zimmerman et al., 2012). Together with the prefrontal cortex dysfunction, poor

executive function may affect performance of episodic memory because these are critical for encoding and retrieval of memory (Brand & Markowitsch, 2008). The deficits of the prefrontal cortex and executive function may influence episodic memory (Parks et al., 2011).

A further effect of sleep problems can be seen in relation to cognitive reserve. Poor sleep may increase negative neuroplasticity (e.g., decrease in dendritic connection or decline of brain size), which influences other cognitive functions (e.g., memory, attention, and episodic memory) (Vance et al., 2010). It is possible that cognitive reserve may be associated with the relationship between sleep disturbances and episodic memory in older adults but this inference needs further investigation.

In addition to attention, executive function, and cognitive reserve, sleep disturbances is significantly associated with depressive symptoms in older adults. Older adults with greater depressive symptoms have increased sleep disturbances (i.e. reduced sleep efficiency, increased sleep latency, longer fragmented sleep episodes, more number of fragmented sleep episodes, poor sleep quality, and increased daytime sleepiness) (Maglione et al., 2012; Paudel et al., 2008). On the other hand, individuals with poor sleep have more depressive symptoms (Nebes et al., 2009). In summary, sleep disturbances and depressive symptoms are correlated with each other.

This review of the literature has revealed some knowledge gaps. It is known that attention and executive function, which are affected by sleep disturbances, may be correlated with episodic memory in older adults. However, there are few studies that investigated the effect of attention and executive function on the relationship between sleep disturbances and episodic memory among older adults. Although Vance and her colleagues inferred that poor sleep may contribute to decline of cognitive reserve (Vance et al., 2010), in this literature review, no studies were found that clearly indicated the effect of sleep on cognitive reserve and the effects

of cognitive reserve in combination with sleep disturbances on episodic memory. Although it is known that depressive symptoms are significantly associated with episodic memory declines (Beaudreau & O'Hara, 2009; Gonzalez et al., 2008; Panza et al., 2009) and sleep disturbances (Maglione et al., 2012; Paudel et al., 2008) among older adults, what remains unclear is the effect of depressive symptoms on the relationship between sleep disturbances and episodic memory in older adults. It is clear that aging is significantly related to sleep disturbances and declines of episodic memory. However, the role of aging in the relationship of sleep disturbances and episodic memory performance is unknown. Thus, more studies are needed to evaluate the relationship between sleep disturbances and episodic memory and the role of attention, executive function, cognitive research function, aging, and depressive symptoms in this relationship.

To address these knowledge gaps, a conceptual framework was constructed to demonstrate the relationship between sleep disturbances and episodic memory and possible roles of the other related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve) in older adults, which is shown in Figure 4.1. The dotted lines indicate knowledge gaps.

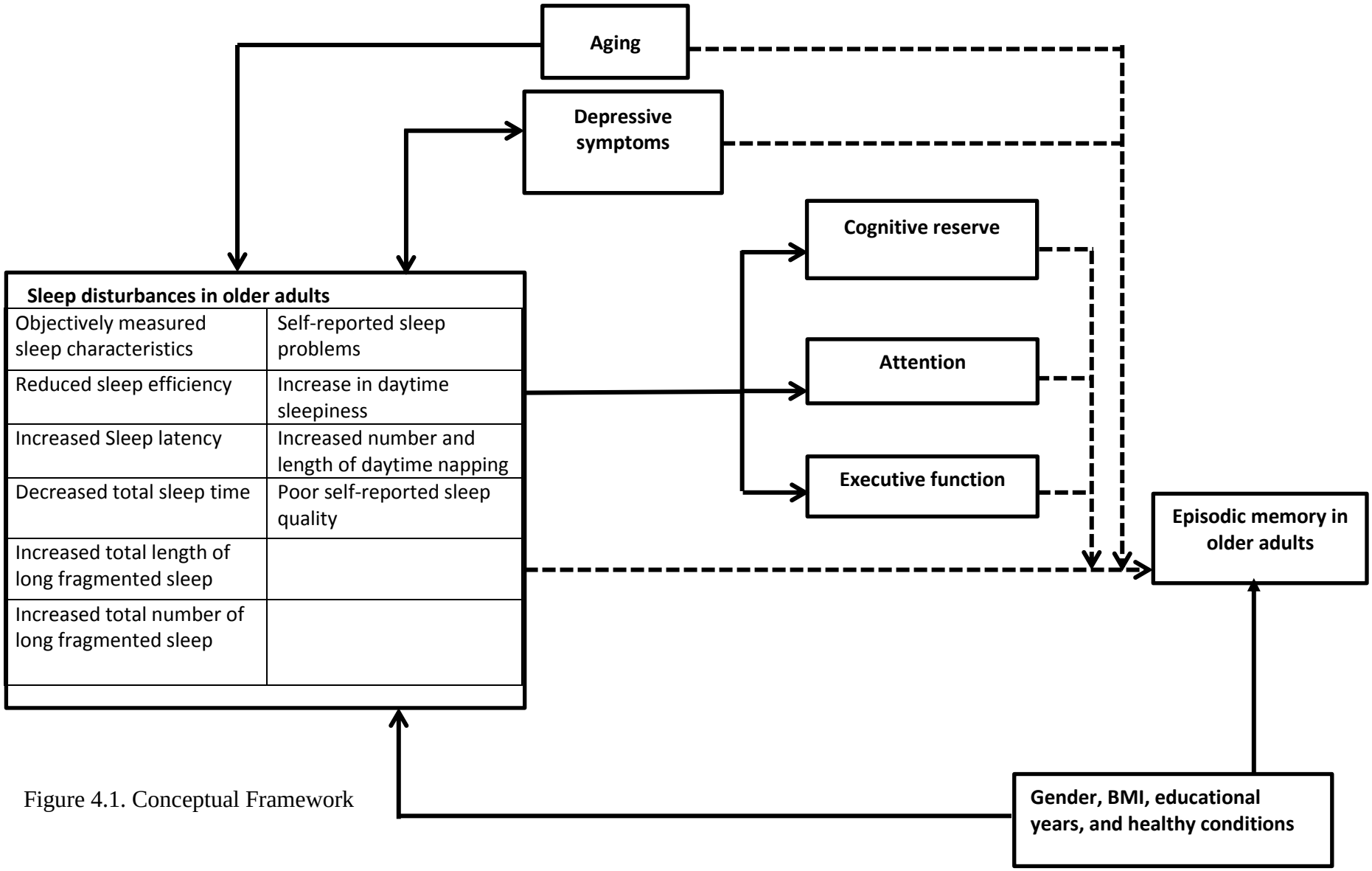

Figure 4.1. Conceptual Framework

Following this framework, the aims of this research were to determine 1) which sleep characteristics both self-reported and objectively measured characteristics, are more likely correlated with episodic memory , 2) whether those sleep characteristics and related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve) can explain the episodic memory performance, 3) the roles of age, depressive symptoms, attention, executive function, and cognitive reserve in the relationship between sleep disturbances and episodic memory in older adults. It is hypothesized that sleep characteristics and related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve) can explain the episodic memory in older adults and that age, depressive symptoms, attention, executive function, and cognitive reserve can affect the relationship between sleep disturbances and episodic memory in older adults.

Method

Sample and Settings

This was a cross-sectional (Brink & Wood, 1998) descriptive study (Grimes & Schulz, 2002). Approval from the Institutional Review Board (IRB) of University of Michigan was obtained before initializing data collection. Following IRB approval, possible participants were recruited from the Michigan Alzheimer's Disease Center at Ann Arbor, Michigan and the database of the UMClinicalStudies.org. The possible participants were screened for eligibility based on inclusion and exclusion criteria after they provided their informed consent to participate in this research.

The inclusion criteria included were as follows (1) healthy older adults 60 years and older (Cansino, 2009), (2) native English speaker, (3) able to tolerate wearing an actigraph devices, and (4) having sufficient visual and auditory function for communication. The exclusion criteria

included (1) neurological disorders: Alzheimer's disease or other type of diagnosed dementia, neurodegenerative disorders (i.e., Parkinson's disease, Huntington's disease, and multiple sclerosis), traumatic brain injury with consciousness loss > 30minutes, epilepsy, stroke, a score on the Montreal Cognitive Assessment (MoCA) < 21, (2) active psychiatric problems based on DSM-V : major psychiatric disorders (i.e., bipolar disorder, schizophrenia, and major depression), substance abuse (i.e., illicit drug), the score of the brief Michigan Alcoholism Screening Test-Revised (bMAST) ≥ 6, and (3) chronic medical problems: heart failure, diagnosed sleep disorders, sleep apnea with continuous positive airway pressure therapy, end-stage renal disease with dialysis therapy, severe liver disease (i.e., liver cirrhosis and hepatic cancer), and current cancer with chemotherapy or radiotherapy. The MoCA was used to exclude those with potential Alzheimer's disease or other types of dementia and the bMAST was used to exclude persons with alcoholism.

Measures

Demographic factors and clinical conditions.

Participants' demographic information (i.e., gender, age, race, years of education, marital status, occupation, employment status, medication administration, weekly consumption of alcohol, and caffeine intake) was collected during the first face-to-face interview. Healthy conditions were determined by the Charlson Cormorbidity Index questionnaire. Self-reported body weight and height were collected and used to calculate body mass index (BMI).

Screening tests.

Montreal Cognitive Assessment (MoCA).

In this study, the Montreal Cognitive Assessment (MoCA) was administrated to screen for possible Alzheimer's disease or other types of dementia by measuring global cognitive

function with a cutoff point of 21. The components of the MoCA include the tasks of short-term memory recall, delayed memory recall, visuospatial/executive function, attention, language, abstraction, and orientation. This assessment has good test-retest reliability of the MoCA (r= 0.92, p<.001; Cronbach alpha of 0.83). A good construct validity of the MoCA is revealed by a high correlation between the MoCA and the MMSE (r =0.87, p<.001). The MoCA results for normal control, mild cognitive impairment, and Alzheimer's disease groups were significantly different [F(2, 269) = 183.32, p>.001) after controlling for age and education, indicating good validity (Nasreddine et al., 2005).

Brief Michigan Alcohol Screening Test (bMAST).

The brief Michigan Alcohol Screening Test (bMAST), which consists of 10 yes/no questions was used to screen for alcoholism. The score range for the bMAST is 0 to 29, where a higher total score represents a higher possibility of alcoholism with a cutoff point of 6 (Pokorny et al., 1972). The reliability of this test is acceptable as revealed by a significant correlation between items ranging from 0.23 to 0.64 (p<.01). In an assessment of validity, the results of factor analysis generated two factors: perception of current drinking and drinking consequences which can explain with 56.40% of scale variance. Both of these factors were significantly correlated with the total score of the Alcoholic Use Disorders Identification Test (r= 0.36, p <.01 and r=0.57, p<.01, respectively) (Connor et al., 2007). These results indicate an adequate construct validity of the bMAST.

Sleep disturbances.

Actigraphy.

Wrist actigraphy (ActiGraph, LLC. Pensacola, FL) was utilized to measure sleep disturbances objectively. Actigraphy estimates sleep characteristics by assessing activity levels

during sleep (Sadeh et al., 1995). In this study, recorded actigraphy data were analyzed by ActiLife, the software provided by the actigraphy manufacturer (ActiGraph, LLC, Pensacola, FL) and the Cole-Kripke algorism was utilized to calculate sleep parameters including total sleep duration, total length, average length, and number of wakefulness after sleep onset (WASO), and average length and number of long wakefulness after sleep onset (LWASO) (fragmented sleep episodes > 5 min). Three other sleep parameters namely sleep latency, total bed time, and sleep efficiency were determined by comparing the recorded actigraphy data and the sleep logs (time to bed and time to wake up). The validity and reliability of actigraphy for sleep measures have been well-established. The construct validity of wrist actigraphy is determined by comparing the results from actigraphy and polysomnography. The sleep parameters from the actigraphy and the PSG were significantly correlated (total sleep duration: $r= 0.91$, $p<.0001$; sleep efficiency: $r= 0.85$, $p<.002$; sleep latency: $r= 0.94$, $p<.0001$; the length of fragmented sleep episode: $r= 0.49$, $p <.05$), indicating an acceptable validity (Cole et al., 1992). The test-retest reliability of actigraghy performed in laboratory conditions has been shown to be 0.98, which is adequate (Tryon, 2005). The sleep parameters for seven nights measured by an actigraph device was summed up and then divided by seven to obtain the means of sleep parameters, which were used for statistical analysis

Sleep logs.

The participants used a log to report the time to bed and time getting out of bed, number and length of naps, and self-reported sleep quality during the seven days of wearing the actigraphy. The duration between time to bed and getting out of bed were used to calculate total bed time. By comparing total bed time with total sleep duration obtained from the actigraphy, the sleep efficiency was determined.

Pittsburgh Sleep Quality Index (PSQI).

The Pittsburgh Sleep Quality Index (PSQI) was used to evaluate self-reported sleep disturbances. This questionnaire consists of 19 items responded to by participants and 5 items responded to the by bed partners of participants. These self-reported items can be divided into seven subscales: 1) subjective sleep quality; 2) sleep latency; 3) sleep duration; 4) habitual sleep efficiency; 5) sleep disturbances; 6) use of sleep medications; and 7) daytime dysfunction. Total scores range from 0 to 21 and are used to indicate sleep quality. A higher score indicates poorer sleep quality, with a cut-off point of five indicating poor sleep quality (Buysse et al., 1989). The validity and reliability of the PSQI have been well-established. An adequate internal consistency was demonstrated by a correlation of the score of each subscale to the total score that ranged from 0.24 to 0.62 (Cronbach alpha of 0.78) (Beaudreau et al., 2012). Compared with the individuals without sleep disorders, the patients with sleep disorders (i.e., insomnia, restless legs syndrome, and sleep apnea) had significantly poorer sleep quality measured by the PSQI ($p<.001$) (Beaudreau et al., 2012), supporting an adequate construct validity.

Epworth Sleepiness Scale (ESS).

The Epworth sleepiness Scale (ESS) was used to evaluate daytime sleepiness, one of the characteristics of sleep disturbances in older adults. The participants are asked to rate the likelihood of dozing off under eight common situations on the basis of 4-point Likert scale. The scores of all situations are summed and ranged from 0 to 24. A higher total score represents a higher level of daytime sleepiness with a cutoff point of 10 (Johns, 1991). The evaluation of the reliability of the ESS showed a correlation of each item to total score ranging from 0.3 to 0.51 ($p<.001$) (Cronbach alpha of 0.7) indicating an adequate internal consistency. For the evaluation of validity, greater daytime sleepiness measured by the ESS was correlated with poor sleep

quality measure by the PSQI ($r = 0.13$, $p<.001$) (Spira et al., 2012). Individuals with obstructive sleep apnea syndrome, narcolepsy, and idiopathic hypersomnia had significantly higher level of daytime sleepiness measured by the ESS than healthy individuals (Johns, 1991). These results indicate an acceptable construct validity of the ESS.

Depressive symptoms.

The Geriatric Depression Scale-short form (GDS-S), which consists of 15 yes/no, questions was used to evaluate depressive symptoms in this study. A higher total score is indicative of more depressive symptoms. Comparison of sensitivity and specificity of the GDS-S with three clinical diagnostic systems: Diagnostic and Statistical Manual of Mental Disorders (DSM)-III and -IV, Computerized diagnostic algorithm of the Geriatric Mental Status Schedule, and International Classification of Diseases-10 showed a sensitivity of 0.805 and a specificity of 0.75. A total score over five suggests the existence of major depression (Wancata et al., 2006).

Episodic memory.

The Hopkins Verbal Learning Test-Revised (HVLT-R) was used to measure episodic memory. This instrument is a word learning test consisting of 12 words that can be classified into one of three semantic categories and includes three learning trials (trial 1, 2, and 3), followed by a delayed recall after a 20 to 25 minutes break (trial 4) and a 24-word recognition test. The results of this test include correct response of trial 1, 2, 3, and delayed recall (trial 4), learning effect (total correct response of trial 1, 2, and 3), representing learning effect, percent retention, and delay recognition. Recognition scores include true-positive response, false-positive response, and a retention discrimination index (true-positive-false positive) (Lezak, Howieson, & Loring, 2004). The reliability and validity of the HVLT-R have been well-established. The test-retest reliability correlation coefficients ranged from 0.537 (recognition discrimination index) to 0.818

(free delayed recall) ($p<.05$) and mean score differences ranged from -0.861 (retention) to 0.800 (retention T-score) ($p>.05$), indicating acceptable reliability (O'Neil-Pirozzi, Goldstein, Strangman, & Glenn, 2012). Studies of the validity demonstrated the results of the HVLT-R were significantly correlated with results of the Wechsler Memory Scale ranged from $r=0.54$ to 0.77 ($p<.001$). Compared with healthy individuals, Alzheimer patients had significantly poorer performance in all results of the HVLT-R (i.e., total recall, delayed recall, retention percentage, and discrimination index) (all $p<.001$) (Shapiro, Benedict, Schretlen, & Brandt, 1999). These results indicate an acceptable validity of the HVLT-R.

Attention.

Detection task.

The Detection task, a section of the CogState battery, was used to assess the attention of the participants by using playing cards. During the Detection task, the participants need to press the "Yes" key as soon as possible when a playing card is face up on the screen. The speed of each response in milliseconds is recorded and transformed by log 10 to evaluate attention. A lower score indicates better speed and attention (CogState Limited, 2013a). The reliability and validity of Detection task have been well-established. An adequate test-retest reliability is determined by a significant correlated between two trials of the Detection task ($r= 0.78$, $p <.01$ for healthy control group and $r= 0.71$, $p<.01$ for Alzheimer's patients). Compared with the healthy control group, the patients with Alzheimer's disease and mild cognitive impairment had significantly poorer attention ($p<.05$), which indicates an adequate construct validity of this task (Hammers et al., 2011).

Identification task.

The Identification task, a section of the CogState battery, was used to assess the visual attention. During the Identification task, the participants are asked to press the " Yes" key if the playing card on the screen is red and press the "No" key if the playing card on the screen is not red. The participants are encouraged to respond as soon as possible. The speed of each response in milliseconds is be recorded and transformed by log 10 to evaluate attention. A lower score indicates better speed and attention (CogState Limited, 2013b).The reliability and validity of Identification task have been well-established. An adequate test-retest reliability is determined by a significant correlation between two trials of the Identification task ($r= 0.79$, $p <.01$ for healthy control group and $r= 0.80$, $p<.01$ for Alzheimer's patients). Compared with the healthy control group, the patients with Alzheimer's disease and mild cognitive impairment had significantly poorer attention performance ($p<.05$), indicating support for construct validity of this task (Hammers et al., 2011).

Executive function.

The Groton Maze Learning (GML) test, a section of the CogState battery, was used to assess participants' executive function. During this test, the participants are asked to learn and complete the maze by following the hidden pathway (i.e., 28 steps and 11 turns). The results of total error are recorded to determine executive function (Pietrzak et al., 2008). The reliability and validity of the GML test have been well-established. An adequate test-retest reliability is determined by a significant correlation between the two trials of the GML test among healthy control group ($r= 0.87$, $p<.05$) and schizophrenia patients ($r=0.78$, $p<.05$) (Pietrzak et al., 2009). The results of the GML test were significantly correlated with another neuropsychological test of

executive function, the Paced Auditory Serial Addition test ranged from r= -0.51 to -0.63 ($p<.05$) (Pietrzak, Cohen, & Snyder, 2007), indicating an adequate validity of the GML test.

Cognitive reserve.

The Wide Range Achievement Test 4-Reading subtest (WRAT 4-R) was used to measure cognitive reserve. On this test, respondents are asked to pronounce a 50-word list in order of increasing unfamiliarity and phonological difficulty. The more incorrect pronunciation or naming of word on the list indicates lower cognitive reserve (Manly, Touradji, Tang, & Stern, 2003). The internal consistency of the WRAT 4-R is 0.93 to 0.98 and the test-retest reliability is 0.94, which indicate an adequate reliability (Spitznagel & Tremont, 2005). The construct validity of the WRAT 4-R is determined by correlation of the results from the WRAT 4-R and the Peabody Picture Vocabulary Test-third edition, another measure for cognitive reserve. The outcome showed that the result of the WRAT 4-R was significantly correlated with that of the Peabody Picture Vocabulary Test-third edition ($r=0.79$, $p<.01$), which indicates support for construct validity of this test (Siedlecki et al., 2009).

Procedures

Data collection was completed by two face-to-face interviews one week apart conducted either at the participants' home or the School of Nursing of University of Michigan. During the first interview, the MoCA and bMAST were administrated to screen the potential participants for eligibility after they provided their informed consent to formally join this research. Once eligibility was determined, demographic factors and healthy conditions were collected from participants and instructions for wearing the actigraph device for following seven days were provided. After 7 days of actigraphy measure, during the second interview, the actigraph device was collected after which self-reported sleep questionnaires (i.e., PSQI and ESS) and cognitive

tests were administrated. Participants who completed the data collection procedure were given a 20-dollar give card as incentive and a brochure about healthy sleep.

Statistical Analysis

In this study, IBM SPSS statistics (version 22, Armonk, NY) was utilized to analyze the data. Descriptive statistics were conducted to summarize demographic factors, healthy conditions, all sleep parameters from actigraphy, the PSQI, the ESS, and sleep logs, cognitive variables (i.e., episodic memory, attention, executive function, and cognitive reserve), and depressive symptoms measured by GDS-S. Exploratory factor analysis was conducted to investigate the factor structure and interrelationship among sleep parameters from actigraphy. Principal components method was used to extract factors; eigenvalues over Kaiser's criterion of >1 and scree plot were used to determine factor numbers; and the Varimax method was used to rotate factor loadings (Polit, 2010). Factor scores of sleep parameters obtained from actigraphy were created by regression method for analysis.

To address Aim 1, Pearson's correlation was computed between sleep parameters and episodic memory performance. To address Aim 2, hierarchical multiple regression was conducted to investigate whether sleep parameters, age, depressive symptoms, attention, executive function, and cognitive reserve explain episodic memory after controlling covariates (i.e., gender, educational years, BMI, and healthy conditions). The results of the HVLT-R (i.e., a delayed recall, the learning effect, and true positive response) were entered as dependent variables. Independent variables included sleep parameters (i.e., sleep factors from actigraphy, sleep quality measured by the PSQI, and daytime sleepiness measured by the ESS), age, depressive symptoms, attention measured by the Detection and Identification task, executive function measured by the GML test, and cognitive reserve measured by the WRAT 4-R. Gender,

educational years, BMI, and healthy conditions were entered as covariates. P value <.05 was used to determine significant level (Polit, 2010). To address Aim 3, Pearson's correlation, simultaneous multiple regression analysis, and hierarchical multiple regression analysis were conducted to explore the role (i.e., mediator or moderator) of age, depressive symptoms, attention, executive function, and cognitive reserve in the relationship between sleep parameters and episodic memory in older adults (Baron & Kenny, 1986; Bennett, 2000).

Results

A convenience sample of 62 health older adults was recruited for this study. The demographic factors of this sample are shown in Table 4.2. The majority of participants were female (75%), White (87%), retired (66 %) and had a bachelor's degree or higher (90%); mean age was around 69 years old; around 21% had not drunk any alcohol for past 30 days; no one currently smoked cigarettes or chewed tobacco; and just over 30% had hypertension or hyperlipidemia. All participants completed the PSQI and the ESS questionnaires and all cognitive assessments. Fifty-six (90 %) completed the 7-night actigraphic sleep assessment and sleep logs; 5 (8%) wore the actigraph device for only 6 nights; and one (2%) wore this device for only 5 nights due to forgetfulness or visiting of emergency room for healthy problems. The means of the sleep parameters from the actigraphy were used for analysis. The results from the PSQI, the ESS, actigraphy, and sleep logs are shown in Table 4.2. As can be seen, six of the participants took over-the counter medications (i.e., melatonin and diphenhydramine (BENADRYL®) for sleep; over 40% had poor sleep quality (total PSQI score > 5); only around 8 % had excessive daytime sleepiness (total score of ESS > 10); and 50% had taken daytime naps in the duration of data collection.

Table 4.2.

Descriptive Statistics for Sample Characteristics and Sleep Parameters (N=62; male/female= 17/47)

Variables	N (%)	Mean (SD)	Median	Range
Age (years)		69.9 (7.1)	68.50	60-88
Educational years		18.2 (3.1)	18.00	12-28
Educational level				
High school	4 (6.5)			
Trade school or associate degree	2 (3.2)			
Bachelor	25 (40.3)			
Master	20 (32.3)			
Doctoral	11 (17.7)			
Race				
White	54 (87.1)			
African American	6 (9.7)			
Asian	1 (1.6)			
More than one race	1(1.6)			
BMI		26.1 (4.8)	25.20	18.5-43.4
Smoking history (pack years)		25.3 (34.5)	7.50	0.0-140
Days drinking alcohol / 30 days		7.2 (8.6)	3.75	0-30
Coffee / day (cups=8 oz.)		1.6 (1.7)	1.50	0.0-7.0

(continued)

Table 4.2 (continued)

Variables	N (%)	Mean (SD)	Median	Range
Tea / day (cup=8oz.)		0.8 (1.1)	0.18	0.0-5.5
Cola /day (cup=8oz.)		0.4 (1.0)	0.00	0.0-6.0
Charlson Comorbidity Index		0.4 (0.7)	0.00	0.0-3.0
Chronic diseases				
Number of chronic diseases		1.8 (1.4)	2.0	0.0-6.0
Hypertensions	23 (37.1)			
Hyperlipidemia	21(33.9)			
Myocardial infarction	7 (11.3)			
Diabetes	7(11.3)			
Chronic obstructive pulmonary disease	4 (6.5)			
Medication administration				
Taking prescribed medications	51 (82.3)			
Taking OTC medications	57 (91.9)			
Taking melatonin	1 (1.6)			
Taking diphenhydramine (BENADRYL®)	5 (8.1)			
Geriatric Depression Scale		1.2 (2.1)	0.0	0.0-14.0

(continued)

Table 4.2 (continued)

Variables	N (%)	Mean (SD)	Median	Range
Sleep disturbances				
PSQI				
Total score		5.2 (2.9)	5.00	1.0-14.0
Total score > 5	27 (43.5)			
ESS				
Total score		5.3 (3.2)	5.00	0.0-13.0
Total score >10	5 (8.1)			
Actigraphy				
Sleep latency (minutes)		3.5 (4.0)	2.79	0.0-26.4
Sleep efficiency (%)		89.6 (5.0)	90.80	72.2-96.3
Total bed time (hours)		7.8 (0.9)	7.83	5.8-9.5
Total sleep duration (hours)		7.0 (0.8)	6.90	5.0-8.8
Total length of WASO (minutes)		45.8 (24.9)	40.86	15.0-134.8
Numbers of WASO		12.5 (4.4)	11.86	5.4-23.7
Average length of each WASO (minutes)		3.6 (1.1)	3.31	2.0-7.0
Numbers of long WASO (WASO>5 min) (minutes)		3.2 (1.8)	2.71	0.7-9.3
Average length of each long WASO (WASO>5 min) (minutes)		9.0(2.1)	8.77	5.1-15.7

(continued)

Table 4.2 (continued)

Variables	N (%)	Mean (SD)	Median	Range
Sleep logs				
Taking naps	31 (50%)			
Length of naps /day (minutes)		4.8 (12.9)	0.41	0.0-89.4

Note, BMI=body mass index; OTC= over-the-counter; PSQI= Pittsburgh Sleep Quality Index; ESS=Epworth Sleepiness Scale; WASO= Wakefulness after sleep onset

The results of exploratory factor analysis of the sleep parameters from the actigraphy are reported in chapter three. The factor scores were created for data analysis by regression method. The results of cognitive function measures (i.e., episodic memory measured by the HVLT-R, attention measured by the Detection and Identification tasks, executive function measured by the GML test, and cognitive reserve measured by the WRAT 4-R) are shown in Table 4.3.

The results of Pearson's correlation are shown in Table 4.4. Objective difficulty in falling and staying asleep (factor 2) obtained from actigraphy was significantly correlated with the HVLT-R learning effect in this sample ($r= -0.25$, $p<.05$). The total ESS scores which indicated daytime sleepiness, was significantly correlated with the HVLT-R delayed recall ($r= 0.26$, $p<.05$), true positive response ($r= 0.27$, $p<.05$), and learning effect ($r=0.31$, $p<.05$). Age was significantly correlated with the HVLT-R delayed recall ($r= -0.35$, $p<.01$) and learning effect ($r=-0.27$, $p<.05$). The speed of completing the Identification task which indicated attention was significantly correlated with the HVLT-R delayed recall ($r=- 0.28$, $p<.05$). The total errors on the GML test which measured executive function was significantly and negatively correlated with the HVLT-R delayed recall ($r= -0.47$, $p<.01$) and learning effect ($r= -0.38$, $p<.01$). The results of the WRAT 4-R, which measured cognitive reserve, were significantly correlated with the HVLT-R delayed recall ($r= 0.47$, $p<.01$) and learning effect ($r=0.33$, $p<.01$). The total GDS score, which measured depressive symptoms, was significantly and negatively correlated with the HVLT-R delayed recall ($r= -0.42$, $p<.01$).

The results of all hierarchical multiple regressions are shown in Table 4.5. In the first model, the HVLT-R delayed recall was entered as a dependent variable. The independent variables included sleep disturbances (i.e., sleep factors obtained from actigraphy, sleep quality measured by the PSQI, and daytime sleepiness measured by the ESS), age, depressive symptoms,

attention measured by the Detection and the Identification tasks, executive function measured by the total errors on the GML test, and cognitive reserve measured by the WRAT 4-R. Gender, years of education, BMI, and healthy conditions were entered as covariates. The results showed that after controlling for the covariates, this model significantly explained the HVLT-R delayed recall [Overall R^2 = .68, Adjusted R^2 = .57, Δ R^2= 0.38, F (15, 46) = 6.40, p=.000]. Daytime sleepiness (β= 0.20, p=.038), executive function (β= -0.30, p=.007), and cognitive reserve (β= 0.33, p=.003) were independent predictors of the HVLT-R delayed recall. These results indicate that better executive function, higher cognitive reserve , and unexpectedly higher level of daytime sleepiness explained better episodic memory performance among healthy older adults after excluding the influence from covariates.

In the second model, the HVLT-R learning effect was entered as a dependent variable. The independent variables included sleep disturbances (i.e., sleep factors obtained from actigraphy, sleep quality measured by the PSQI, and daytime sleepiness measured by ESS), age, depressive symptoms, attention measured by the Detection and the Identification task, executive function measured by the total errors on the GML test, and cognitive reserve measured by the WRAT 4-R. Gender, years of education, BMI, and healthy conditions were entered as the covariates. The results showed that after controlling for the covariates, this model significantly explained the HVLT-R learning effect [Overall R^2 = .58, Adjusted R^2 = .45, Δ R^2= 0.35, F (15, 46)= 4.29, p=.000]. Objective difficulty in falling and staying asleep (β= -0.22, p=.050), daytime sleepiness (β= 0.24, p=.027), executive function (β= -0.27, p=.028), and cognitive reserve (β= 0.24, p=.050) were independent predictors of the HVLT-R learning effect. These results indicate that, less difficulty in falling and staying asleep, better executive function, higher cognitive

reserve, and unexpectedly higher level of daytime sleepiness explained better episodic memory performance among healthy older adults after excluding the influence from the covariates.

The tests of mediators and moderators demonstrated that only depressive symptoms were a significant moderator between daytime sleepiness and the HVLT-R delayed recall (See Table 4.6). The results of hierarchical multiple regression showed that the interaction term of daytime sleepiness and depressive symptoms was a significant predictor of the HVLT-R delayed recall (β= 1.06, p=.024). This result suggests that compared to the older adults who had less depressive symptoms, the influence of daytime sleepiness in episodic memory was stronger among those who had more depressive symptoms.

Table 4.3

Statistic Results of Cognitive Functions (N=62; male/female= 17/47)

	Variables	Mean (SD)	Median	Range
Episodic memory	Hopkins: delayed recall (trial 4)	10.21 (1.94)	11.00	4.00-12.00
	Hopkins: true positive response	11.66 (0.60)	12.00	10.00-12.00
	Hopkins: semantically-related false positive errors	0.68 (0.88)	0.00	0.00-3.00
	Hopkins: total number of false positive errors	0.68 (0.88)	0.00	0.00-3.00
	Hopkins: learning effect (total correct response of trial 1,2, and 3)	27.66 (4.49)	28.00	17.00-35.00
	Hopkins: retention (%)	94.81 (12.49)	95.84	50.00-125.00
	Hopkins: recognition discrimination index	11.00 (1.04)	11.00	9.00-12.00
Attention	Detection: speed (Log 10 msec)	2.59 (0.72)	2.58	2.46-2.76
	Identification: speed (Log 10 msec)	2.74 (0.05)	2.75	2.64-2.91
Executive function	Groton Maze Leaning test: Total errors	65.48 (21.08)	60.00	35.00-11.00
Cognitive reserve	Wild range achievement test-reading subset score	51.06 (3.78)	52.00	38.00-55.00

Table 4.4

Pearson's Correlations (N=62; male/female= 17/47)

Variables	1	2	3	4	5	6	7	8	9	10	11	12	13
1.Acti_factor 1													
2.Acti_factor 2	.00												
3.Acti_factor 3	.00	.00											
4.PSQI	.35**	.07	.03										
5.ESS	-.03	-.01	-.06	.23									
6.Age	.19	-.26*	.05	.09	-.15								
7.Hopkins_delayed recall	-.06	-.15	-.11	-.10	.26*	-.35**							
8.Hopkins_true positive response	-.05	-.14	-.04	-.04	.27*	-.13	.47**						
9.Hopkins learning effect	-.10	-.25*	-.01	-.09	31*	-.27*	.78**	.48**					
10.DET speed	-.12	-.13	-.07	-.03	.05	.24	-.22	.03	-.12				
11. IDF speed	.13	-.12	.03	.17	.04	.41**	-.28*	.01	-.19	.59**			
12. GML total error	.31*	.10	.04	.05	-.10	.37**	-.47**	-.19	-.38**	-.02	.20		
13. WRAT_R	-.09	.01	-.07	-.04	-.05	-.10	.47**	.22	.33**	-.26*	-.26*	-.33**	
14. GDS	.07	.01	.15	.31*	-.02	.31*	-.42**	-.07	-.24	.21	.44**	.17	-.02

Note. Acti=Actigraphy; PSQI= Pittsburg Sleep Quality Index; ESS= Epworth Sleepiness Scale; RDI= retention discrimination index; DET= Detection; IDF=identification; GML= Groton Maze Learning; WRAT 4-R= Wide Range Achievement Test 4-Reading subtest; GDS= Geriatric Depression Scale.

*p<.05 **p<.01.

Table 4.5
Statistic Results of Hierarchical Multiple Regression (N=62; male/female= 17/47)

Predictors	Episodic memory			
	Delayed recall (Model 1)		Learning effect (Model 2)	
	Step 1	Step 2	Step 1	Step 2
	β		β	
Gender	.19	.28*	.37**	.46**
Educational years	.36**	.26*	.20	.21
Body mass index (kg/m2)	.19	.07	.17	.12
Healthy conditions (Charlson comorbidity index)	-.17	.06	-.01	.17
Factor 1: wakefulness during sleep period		.09		-.00
Factor 2 :difficulty in falling and staying asleep		-.15		-.22*
Factor 3: sleep time		-.01		.05
Sleep quality (PSQI_Total score)		-.02		-.04
Daytime sleepiness (ESS_Total score)		.20*		.24*
Age (years)		-.20		-.20
Attention (Detection_speed)		.03		0.3
Attention (Identification_speed)		.01		-0.6
Executive function (GML_Total error)		-.30**		-.27*
Cognitive reserve (WRAT 4-R)		.33**		.24*
Depressive symptoms (GDS_Total score)		-.12		.08
R^2	.30	.68	.23	.58
Adjusted R^2	.25	.57	.18	.45
ΔR^2		.38		.35
Overall Sig.	.000	.000	.004	.000

Note. Acti=Actigraphy; PSQI= Pittsburg Sleep Quality Index; ESS= Epworth Sleepiness Scale; GML= Groton Maze Learning; WRAT 4-R= Wide Range Achievement test 4-Reading subtest; GDS= Geriatric Depression Scale

*p<.05, **p<.01, ***p<.001.

Table 4.6.

Moderator Test of Depressive Symptoms

Dependent variables: delayed recall

	Predictor variables	b	SE	β	t	p
Step 1	(Constant)	9.84	.45		21.93	.000
	Daytime sleepiness (ESS_Total score)	.15	.07	.25	2.18	.034
	Depressive symptoms (GDS_Total score)	-.37	.10	-.41	-3.62	.001
	Overall R^2 = .24, Adjusted R^2 = .21, F (2, 59)= 9.10, p=.000					
Step 2	(Constant)	10.40	.50		21.01	.000
	Daytime sleepiness (ESS_Total score)	.04	.08	.07	.50	.622
	Depressive symptoms (GDS_Total score)	-1.30	.41	-1.43	-3.16	.002
	Daytime sleepiness × Depressive symptoms	.18	.08	1.06	2.32	.024
	Overall R^2 = .30, Adjusted R^2 = .26, F (3, 58)= 8.31, p=.000					

Note. ESS= Epworth Sleepiness Scale; GDS= Geriatric Depression Scale.

Discussion

The results of this descriptive study demonstrated that episodic memory performance (i.e., delayed recall and learning effect) was significantly correlated with sleep disturbances measured by self-reported questionnaires (i.e., PSQI and ESS) and actigraphy, age, depressive symptoms, attention, executive function, and cognitive reserve . The results of hierarchical multiple regression indicated that episodic memory performance (i.e., delayed recall and learning effect) was significantly explained by the different components of the model (sleep disturbances, age, depressive symptoms, attention, executive function, and cognitive reserve) after controlling for the influence of covariates (i.e., gender, educational years, BMI, and healthy conditions) in older adults. This model explained 38% of the variance of the HVLT-R delayed recall and 35% of the variance of the HVLT-R learning effect. Daytime sleepiness, objective difficulty in falling and staying asleep, executive function, and cognitive reserve were significant predictors of episodic memory. Less difficulty in falling and staying asleep, better executive function, more cognitive reserve , and, unexpectedly, higher levels of daytime sleepiness explained better episodic memory performance in older adults. Depressive symptoms were a significant moderator between sleep disturbances and episodic memory performance in older adults. Compared with the older adults who had less depressive symptoms, the influence of sleep disturbances on episodic memory was stronger among the older adults who had more depressive symptoms. The revised conceptual framework based on the results is shown in Figure 4.2

The results of Pearson's correlation and hierarchical multiple regression indicated that among these significant predictors of episodic memory, daytime sleepiness was more related to

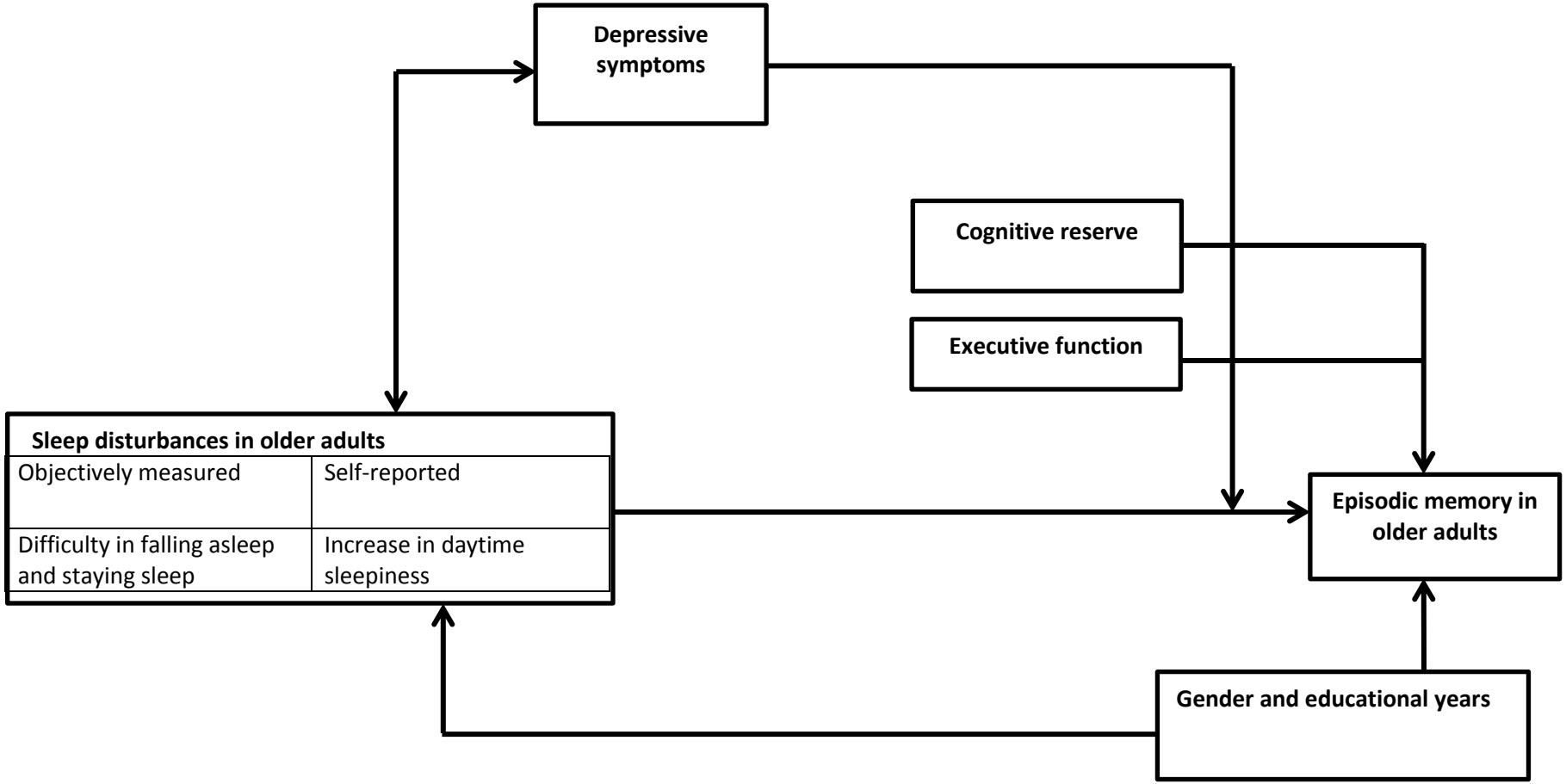

Figure 4.2. Revised Conceptual Framework based on Research Results

episodic memory performances (i.e., free delayed recall and learning effect). The higher level of daytime sleepiness was associated with better episodic memory performance. These results differ from those found in a study by Bonanni et al. (2005) finding that higher levels of daytime sleepiness were related to poorer episodic memory performance (Bonanni et al., 2005). The unexpected result of the present study may be related to the effect of naps. Among this sample, the older adults who took regular naps (50%) had a significantly higher level of daytime sleepiness, suggesting that the episodic memory of older adults who have higher level of daytime sleepiness may benefit from short sleep. In other words, daytime naps might moderate the relationship between daytime sleepiness and episodic memory. Another possible explanation of this unexpected result may be found in the design of the Epworth Sleepiness Scale. This scale asks individuals to report their chances of dozing in 8 situations. This question may have been misunderstood by the respondents. It may be that they thought they were not sleepy in these situations and the ESS score would be low. However, they may feel fatigued, which is associated with impaired episodic memory performance (Xu et al., 2011). Thus, some older adults with lower scores of the ESS indicating lower level of daytime sleepiness had poor episodic memory performance in this study. This inference should be the focus of further investigation, which would add the assessment of fatigue to clarify the effect of daytime sleepiness and fatigue.

In the study by Bonanni et al. (2005), daytime sleepiness was measured objectively by a multiple sleep latency test rather than self-reported questionnaires and this result of daytime sleepiness had a negative correlation with episodic memory performance (Bonanni et al. (2005). However, in this study, there were no objective measures of daytime sleepiness so it not possible to compare the relationship of episodic memory performance and both objective and self-reported measures of daytime sleepiness. Thus, in future studies, objective measures of daytime

sleepiness need to be added to obtain a better understanding of the relationship between daytime sleepiness and episodic memory performance in older adults.

Another sleep disturbance, objective difficulty in falling and staying asleep, was associated with poor episodic memory. This result is consistent with those of previous studies. Three previous studies found that older adults who experience more difficulty in falling asleep or maintaining sleep, longer sleep latency, more sleep fragmentation measured by either self-reported questionnaire and actigraphy had poorer episodic memory performances (Schmutte et al., 2007; Tworoger et al., 2006; Westerberg et al., 2010).

Apart from sleep disturbances, Pearson's correlation demonstrated that better attention was associated with better episodic memory performance. However, unexpectedly, the results of multiple regression showed that attention was not a significant predictor of episodic memory performance. This finding did not support the theoretical framework that proposed that poor attention contributes to impaired episodic memory deficits (Cole & Richards, 2005).

Executive function was associated with episodic memory performance in this study. Better executive function explained better episodic memory performance (i.e., delayed recall and learning effect). This finding provided an empirical support for the theoretical framework that posits that executive function plays an important role in the formation of episodic memory, particularly in encoding and retrieval (Brand & Markowitsch, 2008). Future studies that investigate episodic memory in older adults need to consider the influence of executive function.

In this study, cognitive reserve was significantly related to episodic memory in older adults. More cognitive reserve was associated with better episodic memory performance in these older adults. This result was consistent with a previous study (Vuoksimaa et al., 2013) and supports the theoretical framework that indicates that individuals with more cognitive reserve

can tolerate higher levels of brain lesions than individuals with less cognitive reserve before functional impairment becomes apparent (Stern, 2002).

Depressive symptoms were significantly correlated with episodic memory in this sample; however, depressive symptoms were not a significant predictor of episodic memory. These results are partially consistent with previous studies that demonstrated that depressive symptoms were significantly correlated with deficits of episodic memory (Beaudreau & O'Hara, 2009; Gonzalez et al., 2008; Panza et al., 2009). This association may be attributable to the effect of depression on the hippocampus, the most important brain region for episodic memory. Studies have shown that depression induces hippocampal atrophy, which in turn is associated with declines in episodic memory (Fotuhi et al., 2012). Although depressive symptoms were not significant predictor in this study, it was a significant moderator between sleep disturbances, particularly daytime sleepiness, and episodic memory in older adults. The influence of sleep disturbances on episodic memory was stronger in the older adults with more depressive symptoms. Thus, the future studies which explore the relationship between sleep and episodic memory or even sleep intervention for improving episodic memory should consider the effect of depressive symptoms.

In this study, although age was significantly correlated with objective difficulty in falling and staying asleep and episodic memory performance (i.e., delayed recall and learning effect), it was neither a significant predictor of episodic memory nor a moderator in the relationship between sleep disturbances and episodic memory. These results are not consistent with the findings of previous studies that demonstrated a weaker relationship between sleep and episodic memory in older adults than in young adults, which implies that age might moderate the relationship between sleep and episodic memory (Aly & Moscovitch, 2010; Rauchs et al., 2008;

Spencer et al., 2007; Wilson et al., 2012). This inconsistent result may be explained by the age range of the current study population, which was narrower than that of previous studies, reducing the power of this study to identify the effect of age.

This study has several strengths. First, this study partially supports the theoretical framework constructed based on previous studies finding that sleep disturbances are related to episodic memory in older adults and that age, depressive symptoms, attention, executive function, and cognitive reserve were involved in this memory system. Even in healthy, well-educated, non-depressive older adults, sleep disturbances are still significantly associated with diminished episodic memory. Second, the roles of other cognitive functions (i.e., attention, executive function, and cognitive reserve) in episodic memory performance were investigated, revealing the possibility of the cooperation within the different brain regions to support episodic memory performance. Third, the results of this study indicated that daytime sleepiness and difficulties for falling and staying asleep were more likely associated with episodic memory performance, which may suggest directions for future studies aimed at improving episodic memory by sleep interventions.

Several limitations need to be mentioned. First, there was a selection bias in the sample recruitment. Specifically, the majority of the sample were women (76 %) and White (87 %), had more years of education (18 years), which was higher than mean educational years of adults in the U.S. (12.9 years in 2013) (United Nations, 2013), and was recruited from one area. The second limitation is the sample size. Although the results of the power analysis indicated that 62 participants would provide sufficient power to yield significant results, a larger and more diverse sample would have allow the results to be verified. The third limitation is the lack of longitudinal measures of episodic memory. Future studies should include longitudinal measures of episodic

memory to determine the association between changes of sleep and episodic memory. Such information could contribute to the design of interventions.

Conclusion

This study provides evidence that sleep disturbances and related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve) explained episodic memory performance and found that daytime sleepiness and difficulty in falling and staying asleep were more associated with episodic memory in older adults after excluding the influence from covariates. These results suggest future directions for intervention studies to improve episodic memory through sleep interventions for older adults. Such studies should include more possible factors (i.e., genotype, inflammatory biomarkers, physical activity) that may contribute to a better understanding of the relationship between sleep and episodic memory. Among these related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve), only depressive symptoms were found to influence the relationship between sleep disturbances and episodic memory. Compared with older adults who had less depressive symptoms, the influence of sleep disturbances on episodic memory was stronger in older adult who had more depressive symptoms. Thus, future studies that investigate sleep and episodic memory in older adults should consider the effect of depressive symptoms.

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References

Aly, M., & Moscovitch, M. (2010). The effects of sleep on episodic memory in older and younger adults. *Memory, 18*(3), 327-334. doi: 10.1080/09658211003601548

Backhaus, J., Born, J., Hoeckesfeld, R., Fokuhl, S., Hohagen, F., & Junghanns, K. (2007). Midlife decline in declarative memory consolidation is correlated with a decline in slow wave sleep. *Learning & Memory, 14*(5), 336-341. doi: 10.1101/lm.470507

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51*(6), 1173-1182.

Beaudreau, S. A., & O'Hara, R. (2009). The association of anxiety and depressive symptoms with cognitive performance in community-dwelling older adults. *Psychology and Aging, 24*(2), 507-512. doi: 10.1037/a0016035

Beaudreau, S. A., Spira, A. P., Stewart, A., Kezirian, E. J., Lui, L. Y., Ensrud, K., . . . Stone, K. L. (2012). Validation of the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale in older black and white women. *Sleep Medicine, 13*(1), 36-42. doi: 10.1016/j.sleep.2011.04.005

Beaunieux, H., Hubert, V., Pitel, A. L., Desgranges, B., & Eustache, F. (2009). Episodic memory deficits slow down the dynamics of cognitive procedural learning in normal ageing. *Memory, 17*(2), 197-207. doi: 10.1080/09658210802212010

Bennett, J. A. (2000). Mediator and moderator variables in nursing research: conceptual and statistical differences. *Research in Nursing and Health, 23*(5), 415-420.

Blackwell, T., Yaffe, K., Ancoli-Israel, S., Redline, S., Ensrud, K. E., Stefanick, M. L., . . . Stone, K. L. (2011). Association of sleep characteristics and cognition in older community-dwelling men: the MrOS sleep study. *Sleep, 34*(10), 1347-1356. doi: 10.5665/sleep.1276

Blackwell, T., Yaffe, K., Laffan, A., Ancoli-Israel, S., Redline, S., Ensrud, K. E., . . . Stone, K. L. (2014). Associations of objectively and subjectively measured sleep quality with subsequent cognitive decline in older community-dwelling men: the MrOS sleep study. *Sleep, 37*(4), 655-663. doi: 10.5665/sleep.3562

Bonanni, E., Maestri, M., Tognoni, G., Fabbrini, M., Nucciarone, B., Manca, M. L., . . . Murri, L. (2005). Daytime sleepiness in mild and moderate Alzheimer's disease and its relationship with cognitive impairment. *Journal of Sleep Research, 14*(3), 311-317. doi: 10.1111/j.1365-2869.2005.00462.x

Brand, M., & Markowitsch, H. J. (2008). Chapter 3.5 The role of the prefrontal cortex in episodic memory. *Handbook of behavioral neuroscience: Vol.18.Handbook of episodic memory, 18*, 317-619. doi: 10.1016/s1569-7339(08)00218-x

Brink, P. J., & Wood, M. J. (1998). *Advance Design in Nursing Research*. Thousand Oak, CA: SAGE Publications, Inc.

Burton, C. L., Strauss, E., Hultsch, D. F., & Hunter, M. A. (2006). Cognitive functioning and everyday problem solving in older adults. *The Clinical Neuropsychologist, 20*(3), 432-452. doi: 10.1080/13854040590967063

Buysse, D. J., Reynolds, C. F., 3rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research, 28*(2), 193-213.

Cansino, S. (2009). Episodic memory decay along the adult lifespan: a review of behavioral and neurophysiological evidence. *International Journal of Psychophysiology, 71*(1), 64-69. doi: 10.1016/j.ijpsycho.2008.07.005

Cochrane, A., Robertson, I. H., & Coogan, A. N. (2012). Association between circadian rhythms, sleep and cognitive impairment in healthy older adults: an actigraphic study. *Journal of Neural Transmission, 119*(10), 1233-1239. doi: 10.1007/s00702-012-0802-2

CogState Limited. (2013a, March 13). Detection task [Web message]. Retrieved from http://www.cogstate.com/go/research/our-tasks/detection-task

CogState Limited. (2013b, March 13). Identification task [Web message]. Retrieved from http://www.cogstate.com/go/research/our-tasks/identification-task

Cole, C. S., & Richard, K. C. (2005). Sleep and cognition in people with Alzheimer's disease. *Issue in Mental Health Nursing, 26*(7), 687-698. doi: 10.1080/01612840591008258

Cole, R. J., Kripke, D. F., Gruen, W., Mullaney, D. J., & Gillin, J. C. (1992). Automatic sleep/wake identification from wrist activity. *Sleep, 15*(5), 461-469.

Connor, J. P., Grier, M., Feeney, G. F., & Young, R. M. (2007). The validity of the Brief Michigan Alcohol Screening Test (bMAST) as a problem drinking severity measure. *Journal of Studies on Alcohol and Drugs, 68*(5), 771-779.

Dickerson, B. C., & Eichenbaum, H. (2010). The episodic memory system: neurocircuitry and disorders. *Neuropsychopharmacology, 35*(1), 86-104. doi: 10.1038/npp.2009.126

Fenn, K. M., Gallo, D. A., Margoliash, D., Roediger, H. L., & Nusbaum, H. C. (2009). Reduced false memory after sleep. *Learning & Memory, 16*(9), 509-513. doi: 10.1101/lm.1500808

Ferrie, J. E., Shipley, M. J., Akbaraly, T. N., Marmot, M. G., Kivimaki, M., & Singh-Manoux, A. (2011). Change in sleep duration and cognitive function: findings from the Whitehall II Study. *Sleep, 34*(5), 565-573.

Foley, D. J., Monjan, A. A., Brown, S. L., Simonsick, E. M., Wallace, R. B., & Blazer, D. G. (1995). Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep, 18*(6), 425-432.

Fotuhi, M., Do, D., & Jack, C. (2012). Modifiable factors that alter the size of the hippocampus with ageing. *Nature Reviews.Neurology, 8*(4), 189-202. doi: 10.1038/nrneurol.2012.27

Goldberg, T. E., Koppel, J., Keehlisen, L., Christen, E., Dreses-Werringloer, U., Conejero-Goldberg, C., . . . Davies, P. (2010). Performance-based measures of everyday function in mild cognitive impairment. *The American Journal of Psychiatry, 167*(7), 845-853. doi: 10.1176/appi.ajp.2010.09050692

Gonzalez, H. M., Bowen, M. E., & Fisher, G. G. (2008). Memory decline and depressive symptoms in a nationally representative sample of older adults: the Health and Retirement Study (1998-2004). *Dementia and Geriatric Cognitive Disorders, 25*(3), 266-271. doi: 10.1159/000115976

Grimes, D. A., & Schulz, K. F. (2002). An overview of clinical research: the lay of the land. *Lancet, 359*(9300), 57-61. doi: 10.1016/s0140-6736(02)07283-5

Haimov, I. (2006). Association between memory impairment and insomnia among older adults. *European Journal of Ageing, 3*(2), 107-115. doi: 10.1007/s10433-006-0026-0

Hammers, D., Spurgeon, E., Ryan, K., Persad, C., Heidebrink, J., Barbas, N., . . . Giordani, B. (2011). Reliability of repeated cognitive assessment of dementia using a brief

computerized battery. *American Journal of Alzheimer's Disease and Other Dementias, 26*(4), 326-333. doi: 10.1177/1533317511411907

Harrison, Y., & Horne, J. A. (1999). One night of sleep loss impairs innovative thinking and flexible decision making. *Organizational Behavior and Human Decision Processes, 78*(2), 128-145.

Harrison, Y., Horne, J. A., & Rothwell, A. (2000). Prefrontal neuropsychological effects of sleep deprivation in young adults--a model for healthy aging? *Sleep, 23*(8), 1067-1073.

Hart, R. P., Morin, C. M., & Best, A. M. (1995). Neuropsychological performance in elderly insomnia patients. *Aging, Neuropsychology, and Cognition, 2*(4), 268-278.

Hornung, O. P., Regen, F., Danker-Hopfe, H., Schredl, M., & Heuser, I. (2007). The relationship between REM sleep and memory consolidation in old age and effects of cholinergic medication. *Biological Psychiatry, 61*(6), 750-757. doi: 10.1016/j.biopsych.2006.08.034

Johns, M. W. (1991). A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep, 14*(6), 540-545.

Kronholm, E., Sallinen, M., Suutama, T., Sulkava, R., Era, P., & Partonen, T. (2009). Self-reported sleep duration and cognitive functioning in the general population. *Journal of Sleep Research, 18*(4), 436-446. doi: 10.1111/j.1365-2869.2009.00765.x

Lavery, L. L., Dodge, H. H., Snitz, B., & Ganguli, M. (2009). Cognitive decline and mortality in a community-based cohort: the Monongahela Valley Independent Elders Survey. *Journal of the American Geriatrics Society, 57*(1), 94-100. doi: 10.1111/j.1532-5415.2008.02052.x

Lee, H. B., Kasper, J. D., Shore, A. D., Yokley, J. L., Black, B. S., & Rabins, P. V. (2006). Level of cognitive impairment predicts mortality in high-risk community samples: the memory

and medical care study. *J Neuropsychiatry Clin Neurosci, 18*(4), 543-546. doi: 10.1176/appi.neuropsych.18.4.543

Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological Assessment*. New York, NY: Oxford University Press, Inc.

Loerbroks, A., Debling, D., Amelang, M., & Sturmer, T. (2010). Nocturnal sleep duration and cognitive impairment in a population-based study of older adults. *nternational Journal of Geriatric Psychiatry, 25*(1), 100-109. doi: 10.1002/gps.2305

Maglione, J. E., Ancoli-Israel, S., Peters, K. W., Paudel, M. L., Yaffe, K., Ensrud, K. E., & Stone, K. L. (2012). Depressive symptoms and subjective and objective sleep in community-dwelling older women. *Journal of the American Geriatrics Society, 60*(4), 635-643. doi: 10.1111/j.1532-5415.2012.03908.x

Manly, J. J., Touradji, P., Tang, M. X., & Stern, Y. (2003). Literacy and memory decline among ethnically diverse elders. *Journal of Clinical and Experimental Neuropsychology, 25*(5), 680-690. doi: 10.1076/jcen.25.5.680.14579

Martin, J. L., Fiorentino, L., Jouldjian, S., Josephson, K. R., & Alessi, C. A. (2010). Sleep quality in residents of assisted living facilities: effect on quality of life, functional status, and depression. *Journal of the American Geriatrics Society, 58*(5), 829-836. doi: 10.1111/j.1532-5415.2010.02815.x

Mazzoni, G., Gori, S., Formicola, G., Gneri, C., Massetani, R., Murri, L., & Salzarulo, P. (1999). Word recall correlates with sleep cycles in elderly subjects. *Journal of Sleep Research, 8*(3), 185-188.

Merritt, P., Hirshman, E., Zamani, S., Hsu, J., & Berrigan, M. (2006). Episodic representations support early semantic learning: evidence from midazolam induced amnesia. *Brain and Cognition, 61*(2), 219-223. doi: 10.1016/j.bandc.2005.12.001

Nasreddine, Z. S., Phillips, N. A., Bedirian, V., Charbonneau, S., Whitehead, V., Collin, I., . . . Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society, 53*(4), 695-699. doi: 10.1111/j.1532-5415.2005.53221.x

Nebes, R. D., Buysse, D. J., Halligan, E. M., Houck, P. R., & Monk, T. H. (2009). Self-reported sleep quality predicts poor cognitive performance in healthy older adults. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences 64*(2), 180-187. doi: 10.1093/geronb/gbn037

Ohayon, M. M., & Vecchierini, M. F. (2002). Daytime sleepiness and cognitive impairment in the elderly population. *Archives of Internal Medicine, 162*(2), 201-208.

O'Neil-Pirozzi, T. M., Goldstein, R., Strangman, G. E., & Glenn, M. B. (2012). Test-re-test reliability of the Hopkins Verbal Learning Test-Revised in individuals with traumatic brain injury. *Brain Injury, 26*(12), 1425-1430. doi: 10.3109/02699052.2012.694561

Oosterman, J. M., van Someren, E. J., Vogels, R. L., Van Harten, B., & Scherder, E. J. (2009). Fragmentation of the rest-activity rhythm correlates with age-related cognitive deficits. *Journal of Sleep Research, 18*(1), 129-135. doi: 10.1111/j.1365-2869.2008.00704.x

Panza, F., D'Introno, A., Colacicco, A. M., Capurso, C., Del Parigi, A., Caselli, R. J., . . . Solfrizzi, V. (2009). Temporal relationship between depressive symptoms and cognitive impairment: the Italian Longitudinal Study on Aging. *Journal of Alzheimer's Disease, 17*(4), 899-911. doi: 10.3233/JAD-2009-1111

Parks, C. M., Iosif, A., Farias, S., Reed, B., Mungas, D., & DeCarli, C. (2011). Executive function mediates effects of white matter hyperintensities on episodic memory. *Neuropsychologia, 49*(10), 2817-2824. doi: D - NLM: NIHMS310100

Paudel, M. L., Taylor, B. C., Diem, S. J., Stone, K. L., Ancoli-Israel, S., Redline, S., . . . Osteoporotic Fractures in Men Study, G. (2008). Association between depressive symptoms and sleep disturbances in community-dwelling older men. *Journal of the American Geriatrics Society, 56*(7), 1228-1235. doi: 10.1111/j.1532-5415.2008.01753.x

Pietrzak, R. H., Cohen, H., & Snyder, P. J. (2007). Spatial learning efficiency and error monitoring in normal aging: an investigation using a novel hidden maze learning test. *Archives of Clinical Neuropsychology, 22*(2), 235-245. doi: 10.1016/j.acn.2007.01.018

Pietrzak, R. H., Maruff, P., Mayes, L. C., Roman, S. A., Sosa, J. A., & Snyder, P. J. (2008). An examination of the construct validity and factor structure of the Groton Maze Learning Test, a new measure of spatial working memory, learning efficiency, and error monitoring. *Archives of Clinical Neuropsychology, 23*(4), 433-445. doi: 10.1016/j.acn.2008.03.002

Pietrzak, R. H., Snyder, P. J., Jackson, C. E., Olver, J., Norman, T., Piskulic, D., & Maruff, P. (2009). Stability of cognitive impairment in chronic schizophrenia over brief and intermediate re-test intervals. *Human Psychopharmacology, 24*(2), 113-121. doi: 10.1002/hup.998

Poe, G. R., Walsh, C. M., & Bjorness, T. E. (2010). Cognitive neuroscience of sleep. *Progress in Brain Research, 185*, 1-19. doi: 10.1016/B978-0-444-53702-7.00001-4

Pokorny, A. D., Miller, B. A., & Kaplan, H. B. (1972). The brief MAST: a shortened version of the Michigan Alcoholism Screening Test. *The American Journal of Psychiatry, 129*(3), 342-345.

Polit, D. F. (2010). *Statistics and Data Analysis for Nursing Research*. Upper Saddle River, NJ: Pearson Education Inc.

Rauchs, G., Desgranges, B., Foret, J., & Eustache, F. (2005). The relationships between memory systems and sleep stages. *Journal of Sleep Research, 14*(2), 123-140. doi: 10.1111/j.1365-2869.2005.00450.x

Rauchs, G., Schabus, M., Parapatics, S., Bertran, F., Clochon, P., Hot, P., . . . Anderer, P. (2008). Is there a link between sleep changes and memory in Alzheimer's disease? *Neuroreport, 19*(11), 1159-1162. doi: 10.1097/WNR.0b013e32830867c4

Rosenzweig, E. S., & Barnes, C. A. (2003). Impact of aging on hippocampal function: plasticity, network dynamics, and cognition. *Progress in Neurobiology, 69*(3), 143-179. doi: 10.1016/s0301-0082(02)00126-0

Sadeh, A., Hauri, P. J., Kripke, D. F., & Lavie, P. (1995). The role of actigraphy in the evaluation of sleep disorders. *Sleep, 18*(4), 288-302.

Schmutte, T., Harris, S., Levin, R., Zweig, R., Katz, M., & Lipton, R. (2007). The relation between cognitive functioning and self-reported sleep complaints in nondemented older adults: results from the Bronx aging study. *Behavioral Sleep Medicine, 5*(1), 39-56. doi: 10.1080/15402000709336725

Shapiro, A. M., Benedict, R. H., Schretlen, D., & Brandt, J. (1999). Construct and concurrent validity of the Hopkins Verbal Learning Test-revised. *The Clinical Neuropsychologist, 13*(3), 348-358. doi: 10.1076/clin.13.3.348.1749

Siedlecki, K. L., Stern, Y., Reuben, A., Sacco, R. L., Elkind, M. S., & Wright, C. B. (2009). Construct validity of cognitive reserve in a multiethnic cohort: The Northern Manhattan Study. *Journal of the International Neuropsychological Society 15*(4), 558-569. doi: 10.1017/s1355617709090857

Spencer, R. M., Gouw, A. M., & Ivry, R. B. (2007). Age-related decline of sleep-dependent consolidation. *Learning & Memory, 14*(7), 480-484. doi: 10.1101/lm.569407

Spira, A. P., Beaudreau, S. A., Stone, K. L., Kezirian, E. J., Lui, L. Y., Redline, S., . . . Osteoporotic Fractures in Men, S. (2012). Reliability and validity of the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale in older men. *The Journals of Gerontology.Series A, Biological Sciences and Medical Sciences, 67*(4), 433-439. doi: 10.1093/gerona/glr172

Spitznagel, M. B., & Tremont, G. (2005). Cognitive reserve and anosognosia in questionable and mild dementia. *Archives of Clinical Neuropsychology, 20*(4), 505-515. doi: 10.1016/j.acn.2004.11.003

Squire, L. R., & Kandel, E. R. (2009). *Memory: from Mind to Molecules*. Greenwood Village, CO: Roberts and Company Publishers.

Stenuit, P. & Kerkhofs, M. (2008). Effects of sleep restriction on cognition in women. *Biological Psychology, 77*(1), 81-88. doi: 10.1016/j.biopsycho.2007.09.011

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society 8*(3), 448-460.

Sutter, C., Zollig, J., Allemand, M., & Martin, M. (2012). Sleep quality and cognitive function in healthy old age: the moderating role of subclinical depression. *Neuropsychology, 26*(6), 768-775. doi: 10.1037/a0030033

Tomaszewski Farias, S., Cahn-Weiner, D. A., Harvey, D. J., Reed, B. R., Mungas, D., Kramer, J. H., & Chui, H. (2009). Longitudinal changes in memory and executive functioning are associated with longitudinal change in instrumental activities of daily living in older adults. *The Clinical Neuropsychologist, 23*(3), 446-461. doi: 10.1080/13854040802360558

Tryon, W. W. (2005). The reliability and validity of two ambulatory monitoring actipraphs. *Behavior Research Methods, 37*(3), 492-497.

Tworoger, S. S., Lee, S., Schernhammer, E. S., & Grodstein, F. (2006). The association of self-reported sleep duration, difficulty in sleeping, and snoring with cognitive function in older women. *Alzheimer Disease and Associated Disorders, 20*(1), 41-48. doi: 10.1097/01.wad.0000201850.52707.80

United Nations (2013), United nations development programe:Human Development Reports. 09 April 2015. Retrieved from http://hdr.undp.org/en/content/mean-years-schooling-adults-years

Van Der Werf, Y. D., Altena, E., Vis, J. C., Koene, T., & Van Someren, E. J. (2011). Reduction of nocturnal slow-wave activity affects daytime vigilance lapses and memory encoding but not reaction time or implicit learning. *Progress in Brain Research, 193*, 245-255. doi: 10.1016/B978-0-444-53839-0.00016-8

Vance, D. E., Roberson, A. J., McGuinness, T. M., & Fazeli, P. L. (2010). How neuroplasticity and cognitive reserve protect cognitive functioning. *Journal of Psychosocial Nursing and Mental Health Services, 48*(4), 23-30. doi: 10.3928/02793695-20100302-01

Vuoksimaa, E., Panizzon, M. S., Chen, C. H., Eyler, L. T., Fennema-Notestine, C., Fiecas, M. J., . . . Kremen, W. S. (2013). Cognitive reserve moderates the association between

hippocampal volume and episodic memory in middle age. *Neuropsychologia*, *51*(6), 1124-1131. doi: 10.1016/j.neuropsychologia.2013.02.022

Wancata, J., Alexandrowicz, R., Marquart, B., Weiss, M., & Friedrich, F. (2006). The criterion validity of the Geriatric Depression Scale: a systematic review. *Acta Psychiatrica Scandinavica*, *114*(6), 398-410. doi: 10.1111/j.1600-0447.2006.00888.x

Westerberg, C. E., Lundgren, E. M., Florczak, S. M., Mesulam, M. M., Weintraub, S., Zee, P. C., & Paller, K. A. (2010). Sleep influences the severity of memory disruption in amnestic mild cognitive impairment: results from sleep self-assessment and continuous activity monitoring. *Alzheimer Disease and Associated Disorders*, *24*(4), 325-333. doi: 10.1097/WAD.0b013e3181e30846

Wilson, J. K., Baran, B., Pace-Schott, E. F., Ivry, R. B., & Spencer, R. M. (2012). Sleep modulates word-pair learning but not motor sequence learning in healthy older adults. *Neurobiology of Aging*, *33*(5), 991-1000. doi: 10.1016/j.neurobiolaging.2011.06.029

Xu, L., Jiang, C. Q., Lam, T. H., Liu, B., Jin, Y. L., Zhu, T., . . . Thomas, G. N. (2011). Short or long sleep duration is associated with memory impairment in older Chinese: the Guangzhou Biobank Cohort Study. *Sleep*, *34*(5), 575-580.

Zimmerman, M. E., Bigal, M. E., Katz, M. J., Brickman, A. M., & Lipton, R. B. (2012). Sleep onset/maintenance difficulties and cognitive function in nondemented older adults: the role of cognitive reserve. *Journal of the International Neuropsychological Society*, *18*(3), 461-470. doi: 10.1017/S1355617711001901

Chapter Five

Summary and Conclusions

The primary purposes of this research were to determine which sleep characteristics, both self-reported and objective measures, most strongly correlated with episodic memory performance in healthy older adults and whether those sleep characteristics and related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve) can explain the episodic memory performance in this population. The secondary purpose of this study was to determine the factor structure among sleep parameters obtained via actigraphy and the further association between self-reported and objectively measured sleep disturbances among older adults.

The theoretical framework developed for this research is based on the critical role of sleep (i.e., REM and NREM sleep) in the consolidation and encoding episodic memory as described in previous neuroscience studies. This framework is supported by research that showed that total and partial sleep deprivation may contribute to a decline in episodic memory. Given the evidence, it was reasonable to infer that sleep disturbances may be associated with episodic memory decline. In older adults, age-related sleep disturbances and decline of episodic memory are common problems. Therefore, the hypothesis of this study was that sleep disturbances in older adults are associated with a decline in episodic memory. To examine this hypothesis, sleep disturbances were objectively measured by actigraphy and two self-reported questionnaires. Episodic memory was measured using the Hopkins Verbal Learning Test. In addition to sleep disturbances, the roles of other related factors (i.e., age, depressive symptoms, attention,

executive function, and cognitive reserve) which were related to either sleep disturbances or episodic memory were explored in this study.

In chapter two, the results of a systematic literature review that examed the current knowledge body and gaps are presented. A total of 29 publications were reviewed and critiqued. Results showed that both self-reported and objectively measured sleep disturbances were related to episodic memory in older adults. Importantly, self-reported sleep time had a reverse U-shape association with episodic memory. However, it was unclear whether self-reported or objectively measured sleep disturbances were most strongly associated with episodic memory performance, whether sleep problems explained episodic memory performance, and what role related factors such as age, depressive symptoms, attention, executive function, and cognitive reserve play in this relationship. Self-reported and objectively measured sleep were significantly, but weakly correlated with each other. The existence of a factor structure in objectively measured sleep variables remains unclear from the literature review.

In chapter three, the relationship between self-reported sleep disturbances and actigraphic measured sleep parameters was investigated. First, the factor structure among the actigraphic measured sleep parameters was evaluated using exploratory factor analysis. The results showed that these sleep parameters fit a three-factor solution that explained 86 % of variance. This analysis of the data obtained via actigraphy revealed three important domains of sleep disturbances in older adults: wakefulness during sleep periods, difficulty in falling and staying asleep, and sleep time. Second, the evaluation of the association between self-reported sleep disturbances and the three sleep factors revealed by actigarphy was conducted. The results showed that in this sample, self-reported sleep parameters significantly explained wakefulness during sleep periods and sleep time from actigraphy, after excluding the influence of covariates

(i.e., gender, depressive symptoms, and healthy conditions). However, among the actigraphic measured results, only sleep time was substantially explained by self-reported sleep parameters (64% of variance), indicating that self-reported sleep parameters are substantially associated with objective sleep time among older adults. Although wakefulness during sleep periods revealed by actigraphy was significantly explained by self-reported sleep parameters, the variance was only 23% to 24%. This indicates that it may be hard to substantially predict objective wakefulness during sleep periods from self-reported sleep parameters. The factor of difficulty in falling and staying asleep as revealed by actigraphy was more independent of self-reported sleep parameters.

In chapter four, the relationship between sleep disturbances and episodic memory and the role of related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve) in this relationship were investigated among older adults. The hypothesis in this work proposed that the sleep disturbances were related to episodic memory and these related factors may be associated with episodic memory in older adults. This hypothesis was accepted in this sample. The results indicated that the model including self-reported and actigraphic measured sleep parameters, age, depressive symptoms, attention, executive function, and cognitive reserve significantly explained episodic memory (i.e., delayed recall and learning effect) in older adults. In particular, daytime sleepiness, difficulty in falling and staying asleep, executive function, and cognitive reserve were significant predictors of episodic memory. Greater difficulty in falling and staying asleep, worse executive function, less cognitive reserve, but lower level of daytime sleepiness were associated with poorer episodic memory. Among these related factors, depressive symptoms were a significant moderator between sleep disturbances and episodic memory, indicating that in the older adults with more depressive symptoms, the relationship between sleep disturbances and episodic memory was stronger. The

revised theoretical framework which is shown in Figure 5.1 is based on the above-mentioned research results to be constructed.

The findings of this study contribute to the current scientific body of knowledge about sleep and episodic memory in eight important ways. First, the conclusions of the systematic literature review supported the conclusion that more sleep disturbances are related to poorer episodic memory in older adults. Second, self-reported sleep time formed a reverse U-shape association with episodic memory, indicating that too short and too long sleep times contribute to a decline in episodic memory in older adults. Third, this review identified the following knowledge gaps: 1) it remains unclear which sleep characteristics are more strongly correlated with episodic memory; 2) it remains an open question whether the related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve) are involved in the relationship between sleep disturbances and episodic memory; and 3) no clear and testable theory has been proposed that links sleep and episodic memory and integrates possible related factors for more clinically meaningful and successful interventions. Fourth, in this study and to our knowledge, the factor structure of actigraphic measured sleep parameters was investigated for the first time. Although these sleep parameters were obtained from the actigraph device and measure the same phenomenon, they revealed three stable and distinct factors which correspond to three domains of sleep disturbances in older adults: wakefulness during sleep periods, difficulty in falling and staying asleep, and sleep time. Given the small sample, the labeling of factor structures is tentative and needs validation in a larger sample. Fifth, although self-reported sleep disturbances were associated with actigraphic measured sleep parameters, it was difficult to fully understand sleep disturbances in older adults using only a single type of measure. Sixth, in this study, sleep disturbances as well as the related factors (i.e., age, depressive symptoms,

attention, executive function, and cognitive reserve) affected episodic memory performance in older adults after controlling for covariates (i.e., gender, BMI, educational years, and healthy conditions). This finding suggests the possibility of the need for cooperation of different brain regions to support episodic memory performance. Seventh, the findings of this study indicated that daytime sleepiness and difficulty in falling and staying asleep were more likely associated with episodic memory performance, which suggests directions for future studies that try to improve episodic memory by sleep interventions. Eighth, this study found that depressive symptoms influenced the relationship between sleep disturbances and episodic memory, even though individuals in this sample had fewer depressive symptoms and no diagnosed major depression. Future studies should consider the effect of depressive symptoms.

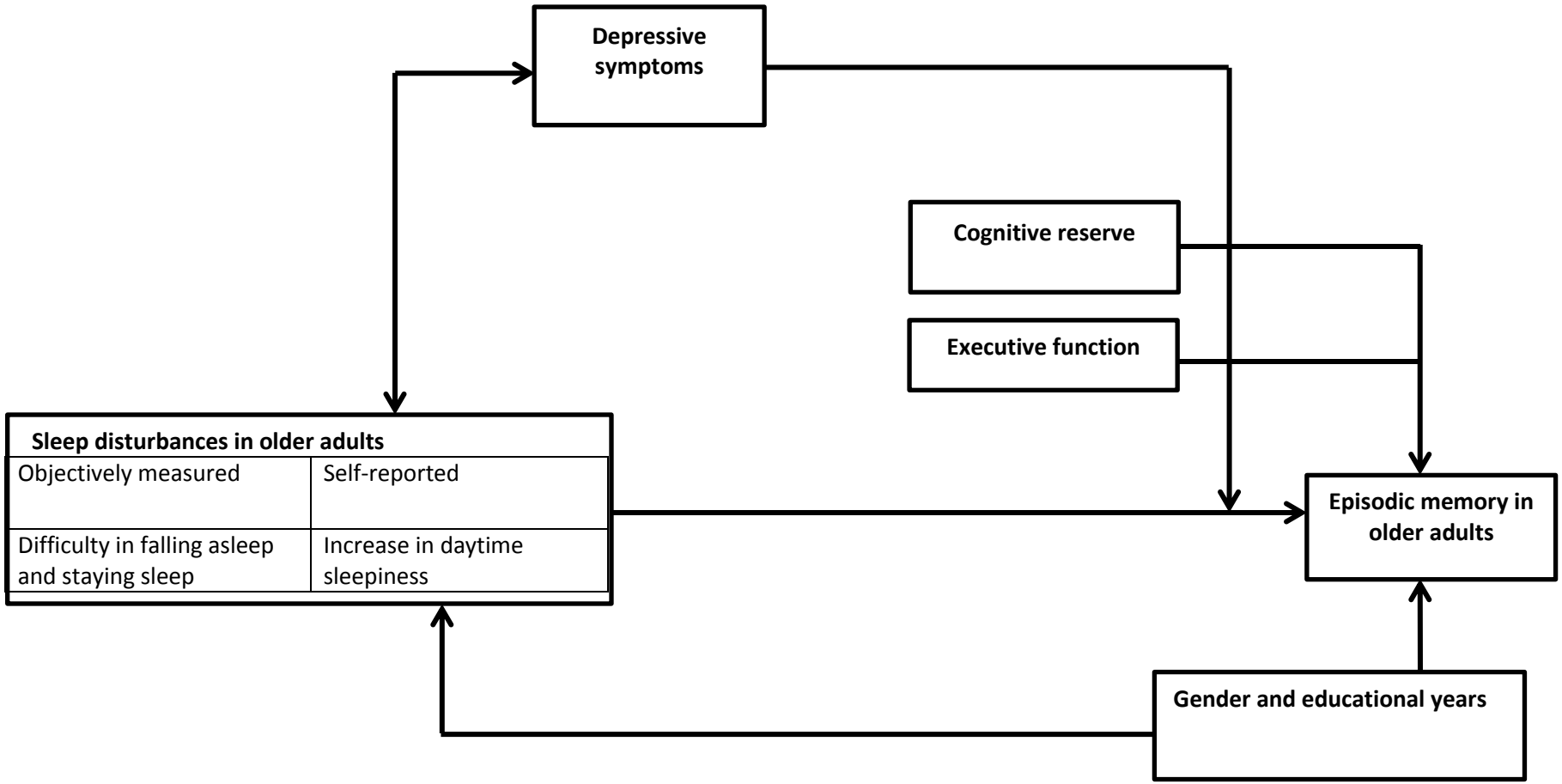

Figure 5.1. Revised Conceptual Framework Based on Research Results

Strength

This study has a number of strengths which should be highlighted. First, in this study, the sleep measures were diverse and included self-reported and objective measures. The use of a diverse set of measures deepens the understanding of sleep disturbances in older adults. Second, possible covariates that may influence sleep or episodic memory were excluded or controlled in this study. Third, the relationship between self-reported and objectively measured sleep disturbances was determined, furthering the understanding of the similarity and diversity of sleep characteristics obtained via different measures. Finally, in this study, the roles of the related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve) were investigated and integrated into the relationship between sleep disturbances and episodic memory, enhancing the understanding of this relationship.

Limitations

Notwithstanding the strengths, this study has a number of limitations. The first one is the selection bias associated with sample recruitment. The sources of selection bias are as follows: the majority of the sample were women (75.8%), White (87.1%), highly educated (18.17 years), which is higher than mean 12.9 educational years of adults in the U.S. (UnitedNations, 2013), and recruited from a single geographical area. The second limitation is the sample size. Although the result of the power analysis indicated that 62 participants were sufficient, a larger and more diverse sample should be obtained in future studies to further investigate the relationship between sleep disturbances and episodic memory. The third limitation was the lack of longitudinal measures of episodic memory.

Implications for the Metaparadigm of Nursing and Nursing Science

The concepts of the metaparadigm of nursing consist of human, health, nursing, and environments (Thorne et al., 1998). These concepts are related to the major investigated variables of this study including sleep and episodic memory. For instance, sleep is involved in human physiological function (Guilleminault & Kreutzer, 2003) and affects human physiological and psychological health. Poor sleep is associated with some environmental factors such as noise (Edwards et al., 2010). The sleep interventions such as sleep hygiene are sensitive to nursing intervention. Episodic memory, another major variable of current study, is one of human cognitive function. Episodic memory is involved in the ability to maintain human health (Burton et al, 2006; Goldberg et al., 2010; Tomaszewski Farias et al., 2009) and to learn new knowledge and skills (Dickerson & Eichenbaum, 2010). Episodic memory may influence the efficiency of health education offered by nurses in clinical settings.

The purpose of this study is consistent with the foci of nursing science which include the holistic health of humans in interactions with the perceived phenomena or factors (e.g., pain or fatigue) that influence human health (National Institute of Nursing Research, 2011; Algase & Whall, 1993), environment (Fuller, 1978), mortality, quality of life, self-management, and health promotion (National Institute of Nursing Research, 2011). According to findings of studies about the above-mentioned domains, nursing researchers develop nursing-sensitive interventions to resolve or mitigate healthy problems and promote health. Sleep and episodic memory both are fundamental for human health (Xiao et al., 2014; Pressler et al., 2010) and influence quality of life (Maki et al., 2014; Manocchia et al., 2001), which is one foci of nursing science and sensitive to nursing interventions. The results of this research contribute to nursing science by shedding light on the relationship between sleep and episodic memory in older adults and the

roles of the other related factors in this relationship. Future studies are needed to develop sleep interventions to prevent declines in episodic memory in this population. One link to possible interventions is the finding that daytime sleepiness and difficulty in falling and staying asleep are more strongly correlated with episodic memory than the other sleep parameters. Executive function and cognitive reserve are involved in episodic memory performance and depressive symptoms influence the relationship between sleep and episodic memory. These results may advance the understanding of this relationship and provide directions for the design of sleep interventions that can be tested by nurses in future studies.

Implications for Future Studies

The results of this study suggest several interesting lines for future studies. First, future studies should include longitudinal measures of episodic memory and sleep in order to investigate the association between changes in sleep disturbances and episodic memory in older adults over time.

Second, biological variables such as inflammatory biomarkers and genotype and physical activity variables may be correlated with sleep and episodic memory. In future studies, the related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive reserve) as well as biological variables such as inflammatory biomarkers, genotype, and physical activity variables could be explored to gain a deeper understating of the relationship between sleep and episodic memory in older adults.

Third, more daytime sleepiness was a significant predictor of better episodic memory, but this association was unexpected. The results indicated that more daytime sleepiness was related to better episodic memory, which is not consistent with a previous study by Bonanni et al. (2005). This lack of agreement may be due to differences in the measures. In the present study, daytime

sleepiness was measured by a self-reported questionnaire, the Epworth Sleepiness Scale while Bonanni et al. (2005) employed objective measures, multiple sleep latency tests. To explore the different outcomes, future studies should add objective measures of daytime sleepiness to further investigate the relationship between daytime sleepiness and episodic memory.

Fourth, a larger and more diverse sample should be the focus of the future studies. This would address the limitation of selection bias in the present study, which was described earlier.

Fifth, the systematic review concluded that self-reported sleep time had a reverse U-shape association with episodic memory in older adults; however, objective sleep time does not show this association with episodic memory. Future work should compare the relationship between self-reported and objective sleep time and episodic memory in older adults to determine the differences between two types of measures of sleep time and possible reasons for demonstrating such reverse U-shape association between sleep time and episodic memory.

Sixth, the correlation between self-reported sleep disturbances and objectively measured sleep parameters was investigated in this study. Although they were correlated, only objective sleep time was substantially explained by self-reported sleep parameters and it seems these two types of measures of sleep reveal different domains of sleep disturbances in older adults. Thus, in future studies, the selection of sleep measures needs to be based on the purposes of the studies.

Implications for Nursing Practice

As the elderly population is growing, age-related sleep disturbances and poor episodic memory will affect more individuals in the U.S. and elsewhere. Since the majority of hospitalized patients are elderly, poor sleep and declines in episodic memory functions are frequently observed by clinical nurses. This research deepens the understanding of the connection between poor sleep and declines in the memory of older adults. This decline is

important because it is associated with decline of functional ability (ADL and IADL) (Burton et al., 2006; Goldberg et al., 2010; Tomaszewski Farias et al., 2009a) and an increased mortality in older adults with (Lee et al., 2006) and without dementia (Lavery et al., 2009). The findings of this study can promote clinical nurses understanding of how poor sleep combined with other related factors relates to declines in episodic memory in older adults, which might be related to abnormal accumulation of amyloid protein in the brain, possible pathological changes of Alzheimer's disease (National Institute on Aging, 2009). Based on the results of this study, clinical nurses can understand the requirement of developing regular long-term and feasible sleep assessments and establishing a referral system to sleep specialists in outpatient clinic settings. In inpatient settings, modification of the clinical environment, schedules to protect patients' sleep time, and health education about sleep hygiene are needed. These may prevent the declines in episodic memory, which in turn can promote functional ability in older adults.

Conclusions

In conclusion, sleep disturbances combined with other related factors (i.e., age, depressive symptoms, attention, executive function, and cognitive function) were associated with poor episodic memory performance in older adults. The relationship between episodic memory and sleep disturbances was moderated by depressive symptoms. These results point to the complexity of the relationship between sleep disturbances and episodic memory and the interaction between different domains of cognitive function, suggesting the possibility of cooperation among different domains of cognitive function. Additionally, although self-reported sleep disturbances were significantly correlated with actigraphic measured sleep parameters, the magnitude of this association was weak. This finding indicates potential differences between

these two types of sleep measures in older adults to obtain more understanding of sleep characteristics.

References

Algase, D. L., & Whall, A. F. (1993). Rosemary Ellis' views on the substantive structure of nursing. *Image the Journal of Nursing Scholarship, 25*(1), 69-72.

Bonanni, E., Maestri, M., Tognoni, G., Fabbrini, M., Nucciarone, B., Manca, M. L., . . . Murri, L. (2005). Daytime sleepiness in mild and moderate Alzheimer's disease and its relationship with cognitive impairment. *Journal of Sleep Research, 14*(3), 311-317. doi: 10.1111/j.1365-2869.2005.00462.x

Burton, C. L., Strauss, E., Hultsch, D. F., & Hunter, M. A. (2006). Cognitive functioning and everyday problem solving in older adults. *The Clinical Neuropsychologist, 20*(3), 432-452. doi: 10.1080/13854040590967063

Dickerson, B. C., & Eichenbaum, H. (2010). The episodic memory system: neurocircuitry and disorders. *Neuropsychopharmacology, 35*(1), 86-104. doi: 10.1038/npp.2009.126

Edwards, B. A., O'Driscoll, D. M., Ali, A., Jordan, A. S., Trinder, J., & Malhotra, A. (2010). Aging and sleep: physiology and pathophysiology. *Seminars in Respiratory and Critical Care Medicine, 31*(5), 618-633. doi: 10.1055/s-0030-1265902

Fuller, S. S. (1978). Holistic man and the science and practice of nursing. *Nursing Outlook, 26*(11), 700-704.

Goldberg, T. E., Koppel, J., Keehlisen, L., Christen, E., Dreses-Werringloer, U., Conejero-Goldberg, C., . . . Davies, P. (2010). Performance-based measures of everyday function in mild cognitive impairment. *The American Journal of Psychiatry, 167*(7), 845-853. doi: 10.1176/appi.ajp.2010.09050692

Guilleminault, C., & Kreutzer, M. L. (2003). Normal sleep. In M. Billiard (Ed.), *Sleep: Physiology, Investigations, and Medicine* (pp. 3-9). New York, NY: Kluwer Academic/Plenum Publisher.

Lavery, L. L., Dodge, H. H., Snitz, B., & Ganguli, M. (2009). Cognitive decline and mortality in a community-based cohort: the Monongahela Valley Independent Elders Survey. *Journal of the American Geriatrics Society, 57*(1), 94-100. doi: 10.1111/j.1532-5415.2008.02052.x

Lee, H. B., Kasper, J. D., Shore, A. D., Yokley, J. L., Black, B. S., & Rabins, P. V. (2006). Level of cognitive impairment predicts mortality in high-risk community samples: the memory and medical care study. *The Journal of Neuropsychiatry and Clinical Neurosciences, 18*(4), 543-546. doi: 10.1176/appi.neuropsych.18.4.543

Maki, Y., Yamaguchi, T., Yamagami, T., Murai, T., Hachisuka, K., Miyamae, F., . . . Yamaguchi, H. (2014). The impact of subjective memory complaints on quality of life in community-dwelling older adults. *Psychogeriatrics, 14*(3), 175-181. doi: 10.1111/psyg.12056

Manocchia, M., Keller, S., & Ware, J. E. (2001). Sleep problems, health-related quality of life, work functioning and health care utilization among the chronically ill. *Quality of Life Research, 10*(4), 331-345.

National Institute of Nursing Research (2011), Bringing Science to Life:NINR Strategic plan. 09 April 2015. Retrived from https://www.ninr.nih.gov/sites/www.ninr.nih.gov/files/ninr-strategic-plan-2011.pdf

National Institute on Aging (2009), Progress Report on Alzheimer's Disease Translating New Knowledge. 05 May 2015. Retrived from

http://www.nia.nih.gov/sites/default/files/2009%20AD%20Progress%20Report%20Final%20B.pdf

Pressler, S. J., Kim, J., Riley, P., Ronis, D. L., & Gradus-Pizlo, I. (2010). Memory dysfunction, psychomotor slowing, and decreased executive function predict mortality in patients with heart failure and low ejection fraction. *Journal of Cardiac Failure, 16*(9), 750-760. doi: 10.1016/j.cardfail.2010.04.007

Thorne, S., Canam, C., Dahinten, S., Hall, W., Henderson, A., & Kirkham, S. R. (1998). Nursing's metaparadigm concepts: disimpacting the debates. *Journal of Advanced Nursing*, 27(6), 1257-1268.

Tomaszewski Farias, S., Cahn-Weiner, D. A., Harvey, D. J., Reed, B. R., Mungas, D., Kramer, J. H., & Chui, H. (2009). Longitudinal changes in memory and executive functioning are associated with longitudinal change in instrumental activities of daily living in older adults. *The Clinical Neuropsychologist, 23*(3), 446-461. doi: 10.1080/13854040802360558

United Nations (2013), United nations development programe:Human Development Reports. 09 April 2015. Retrieved from http://hdr.undp.org/en/content/mean-years-schooling-adults-year