Habitual Sleep Patterns and Prospective Memory in Community-Dwelling Older Adults: Investigating the Roles of Depressive Symptoms and Underlying Cognitive Processes

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Bachelor of Arts (First Class Honours)

This thesis is presented for the degree of Doctor of Philosophy and in partial fulfilment of the requirements for the Master of Clinical Psychology degree at the University of Western Australia

School of Psychological Science

2019
Thesis Declaration

I, Erica Ruth Hodgson, certify that:

This thesis has been substantially accomplished during enrolment in the degree.

This thesis does not contain material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution.

No part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of The University of Western Australia and where applicable, any partner institution responsible for the joint-award of this degree.

This thesis does not contain any material previously published or written by another person, except where due reference has been made in the text.

The work(s) in this thesis are not in any way a violation or infringement of any copyright, trademark, patent, or other rights whatsoever of any person.

Written participant consent was received and archived for all the research involving human data reported in this thesis. All research presented has been assessed and approved by The University of Western Australia Human Research Ethics Committee.

Approval #: RA/4/1/5361.

This thesis contains work that was presented at conferences in poster/oral presentation format, some of which has been co-authored.

Signed:

Date: 02
Abstract

Prospective Memory (PM) refers to planning and executing future intentions. This important ability is needed for a variety of tasks, like paying bills or attending appointments on time. Multiprocess theory proposes that PM tasks vary in their level of cognitive demand, with some tasks processed more automatically (e.g. event-based, remembering to buy milk when passing the shops) and others requiring more strategic monitoring of the environment (e.g. time-based, checking your watch to remember an appointment).

PM may have specific relevance for older adults. Firstly, PM abilities can decline with advancing age. Secondly, older adults may have an increased reliance on PM, e.g. due to increased medical requirements (appointments or medications). Unsurprisingly, better PM abilities in older age are associated with better activities of daily living and quality of life.

One factor that may influence PM abilities in older adults is habitual sleep quality. Sleep quality can decline with age, and may predict performance in attention, executive function and retrospective memory (memory for the past), all of which are important for PM. Moreover, poor sleep is associated with depressive symptoms, which are also associated with poorer PM. It therefore seems likely that sleep is important for PM, either directly or indirectly, but there is little research investigating this.

Aims

The aims of this thesis were 1) to investigate if a relationship exists between habitual sleep and PM in older adults, 2) to investigate if this relationship differs across PM subtypes (event- vs time-based) and, 3) to investigate the potential mechanisms of these relationships (the effect may be via depressive symptoms, attention, executive function or retrospective memory).
Abstract

This thesis contains three studies to assess these aims. In each study, a different method of sleep assessment was considered, with separate, but overlapping, samples of community dwelling older adults (ns = 104-170). Time- and event-based PM, measured using the lab-based, semi-naturalistic Memory for Intentions Screening Test (MIST), were regressed on sleep variables. Participants were also assessed on objective measures of attention, executive function, retrospective memory and self-reported depressive symptoms.

The first study considered self-reported estimates of sleep onset latency (SOL), total sleep time (TST), sleep disturbance and sleep efficiency. Results did not suggest an overall direct relationship between subjective sleep and PM, but found an indirect relationship between sleep (all measures) and PM (both time- and event-based) via depressive symptoms. Another indirect relationship was observed via retrospective memory, but this was only between TST and time-based PM.

The second study assessed sleep objectively using actigraphy, a monitor that estimates sleep (wake after sleep onset, WASO; SOL and TST) using physical movement. Results were generally similar to those in Study 1. While no overall relationships were observed between sleep and PM, indirect paths were observed between sleep (WASO and TST but not SOL) and time-based PM, again via depressive symptoms.

Finally, the third study obtained estimates of sleep architecture from a portable, single electrode electroencephalogram (Zeo). Specific variables considered were WASO, SOL, time in rapid eye movement (REM) and slow wave sleep (SWS). Again, results did not suggest any overall relationships but suggested several indirect relationships between sleep (all measures except REM) and time-based PM via depressive symptoms.
Abstract

Conclusions

This thesis contributes to current knowledge in the field of sleep and PM in older adults. Contrary to hypotheses, results did not suggest a direct relationship between sleep and PM in community older adult samples, regardless of sleep measurement or PM subtype. However, for subjective sleep, results underscored the importance of depressive symptoms, and possibly retrospective memory, in the relationship with PM. For objective sleep, these results again underscored the importance of depressive symptoms, for at least the more demanding PM subtypes.

A strength of this research is that it used multiple, comprehensive evidence-based approaches to assessing sleep and cognitive performance in large samples. It is also encouraging that results were similar across three separate studies, which used varied methods of sleep assessment and broadly separate samples. These findings lay a foundation upon which more experimental paradigms (manipulating sleep, PM or both), and perhaps treatment and intervention studies may be conducted. They also contribute to our growing understanding of the importance of sleep for cognitive function, especially as problems with each often co-occur in older age.
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Author’s Statement of Contribution

All participant data presented were collected as part of the Healthy Ageing Research Program (HARP), co-directed by supervisors Dr Michael Weinborn and Professor Romola Bucks. The candidate was extensively involved in HARP participant recruitment and engagement including speaking at community events, involvement in open days, and contributing to the HARP newsletter. Since enrolment into the PhD program in early 2014, until late 2016, the candidate organised, tested and scored all HARP participants in conjunction with other Psychology PhD and Honours students who were also part of the HARP team. In 2014, the design and initial piloting of the HARP sleep studies were coordinated by the candidate, and the subsequent sleep studies in 2015 and 2016 were administered and scored by the candidate who led a small team of other HARP students in the HARP sleep studies. The candidate assisted in training new PhD and Honours students in the administration of the test battery and sleep equipment, scored participants’ protocols, checked scoring of these protocols, entered and collated data.

Each of the studies contained in this thesis was designed by the candidate in collaboration with her supervisors. The candidate conducted all statistical analyses with guidance from her supervisors, wrote the manuscripts, and made revisions in accordance with feedback provided by supervisors
Authorship Declaration

The papers presented in this thesis have not been prepared for publication. One conference poster presentation and one oral abstract resulted from this thesis (both prepared by the candidate):


In addition to these conference presentations, while completing this thesis, the candidate was a co-author on the following, related research projects:

**Conference Presentations:**


13th International Conference for Cognitive Neuroscience (poster presentation), Amsterdam, The Netherlands.


Journal Publications


I/we certify that author’s statement of contribution, and involvement in each of the works listed above are correct:

(Candidate)

Date: 28.06.2019

Dr. Michael Weinborn

(Coordinating Supervisor -50%)

Date: 28.06.2019

Professor Romola Bucks

(Co-Supervisor -50%)
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>CBT-I</td>
<td>Cognitive Behavioural Therapy for Insomnia</td>
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<td>CI</td>
<td>Confidence Interval</td>
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<td>CSA</td>
<td>Central Sleep Apnoea</td>
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<td>EEG</td>
<td>Electroencephalogram</td>
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<td>EF</td>
<td>Executive Function</td>
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<td>FMRI</td>
<td>Functional Magnetic Resonance Imaging</td>
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<td>HARP</td>
<td>Healthy Ageing Research Program</td>
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<td>MMSE</td>
<td>Mini Mental State Examination</td>
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<td>MPT</td>
<td>Multiprocess Theory</td>
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<td>NART</td>
<td>National Adult Reading Test</td>
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<td>NSF</td>
<td>National Sleep Foundation (United States of America)</td>
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<td>OSA</td>
<td>Obstructive Sleep Apnoea</td>
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<td>PCA</td>
<td>Principal Components Analysis (factor analysis)</td>
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<td>PHQ-9</td>
<td>Patient Health Questionnaire (9 items)</td>
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<tr>
<td>PHQ-8</td>
<td>Patient Health Questionnaire with sleep item removed</td>
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<td>PM</td>
<td>Prospective Memory</td>
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<td>PSG</td>
<td>Polysomnography</td>
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<td>PSQI</td>
<td>Pittsburgh Sleep Quality Questionnaire</td>
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<td>REM</td>
<td>Rapid Eye Movement</td>
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<td>RM</td>
<td>Retrospective Memory</td>
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<tr>
<td>SBSM</td>
<td>Society of Behavioural Sleep Medicine</td>
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<td>SE</td>
<td>Sleep Efficiency</td>
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<td>SOL</td>
<td>Sleep Onset Latency</td>
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<td>SD</td>
<td>Standard Deviation</td>
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<td>SWS</td>
<td>Slow Wave Sleep</td>
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<tr>
<td>TEA TS</td>
<td>Test of Every day Attention, Telephone Search</td>
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<tr>
<td>TST</td>
<td>Total Sleep Time</td>
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<td>UWA</td>
<td>University of Western Australia</td>
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<td>WASO</td>
<td>Wake After Sleep Onset</td>
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Chapter 1: General Introduction
CHAPTER 1

General Introduction

Introduction Overview

This thesis begins by reviewing the literature relevant to prospective memory (PM), sleep and ageing. First, an introduction to PM is presented, which includes a summary of one of the leading PM theories (multiprocess theory; McDaniel & Einstein, 2000). Then the relationship between PM and advancing age is reviewed, considering how PM abilities may change with age and why PM is an important ability in later life. Following this is an introduction to human sleep research, which covers common ways that sleep quality and quantity can be defined and assessed, reasons that interruptions to sleep can occur, relationships between sleep, depressive symptomatology and ageing as well as leading theories regarding how sleep may affect cognitive abilities. Finally, an argument is presented as to why sleep may be important for PM in older age, and the aims, overview and organisation of this thesis are outlined.

Prospective Memory

Prospective Memory (PM) or “remembering to remember” refers to the ability to plan and execute intentions in the future, like buying milk when you pass the shops (McDaniel & Einstein, 2007). This is a complex cognitive process that requires 1) encoding an intention; 2) monitoring the environment for the cue that the task needs to be completed; 3) accurately detecting the relevant cue and 4) correctly recalling and executing the PM intention (McDaniel & Einstein, 2007). Successfully completing a PM task requires abilities in multiple other cognitive domains. Firstly, it involves retrospective memory (memory for the past) to encode, consolidate and retrieve the details of an intention. It also
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requires attentional control to monitor the environment for cues that the task needs to be completed (Kliegel, Martin, McDaniel, & Einstein, 2002; Zimmermann & Meier, 2006). Importantly, PM tasks are often undertaken in the context of an ongoing task (e.g. remembering to turn off the oven in half an hour, while cooking dinner on the stove in the meantime). To achieve this successfully, PM requires abilities in shifting, working memory, and inhibition in order to effectively allocate attention and successfully attend to both tasks (M. Martin, Kliegel, & McDaniel, 2003).

Successful prospective remembering is essential for a range of everyday tasks such as remembering to pay bills, attending an appointment at the correct time, or saying happy birthday to a friend when you see them. These tasks are often completed automatically (McDaniel & Einstein, 2000), however, given the underlying complexities of this domain, PM failures are common (McDaniel & Einstein, 2007). While some of these failures are frustrating, others can be dangerous e.g. forgetting safety behaviours like locking the door or turning off the stove, or forgetting health-related tasks like taking medication at the correct time (Zogg, Woods, Sauceda, Wiebe, & Simoni, 2012).

PM abilities may be specifically important for older adults (Kliegel et al., 2016). Older adults may have an increase in important health-related PM requirements, e.g. increased medication requirements and/or medical appointments. Moreover, given PM’s importance for day-to-day living (grocery shopping, paying bills, household safety), declines in PM abilities could interfere with independent living for this age group (Scullin, Bugg, McDaniel, & Einstein, 2011; Zogg et al., 2012). Indeed, Woods, Weinborn, Velnoweth, Rooney, and Bucks (2012) found that laboratory-tested PM abilities were associated with instrumental activities of everyday living in a sample of community dwelling older
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adults. Unsurprisingly then, PM abilities also appear to influence quality of life in older adults (Woods et al., 2015).

Given that PM is so important for health, safety, independent living and quality of life, especially for older adults, an understanding of factors that influence success in this domain is important. The focus of this program of research is to investigate one important factor that may influence PM in community dwelling older adults: habitual sleep quality.

**Multiprocess theory.**

There have been multiple theoretical models proposed to account for the nature of PM, e.g. the preparatory attentional model (PAM; R. E. Smith, Hunt, McVay, & McConnell, 2007) and the delay model (Heathcote, Loft, & Remington, 2015; Strickland, Loft, Remington, & Heathcote, 2018). Arguably the most widely used model across the PM literature is multiprocess theory (MPT; Einstein et al., 2005; McDaniel & Einstein, 2000; McDaniel & Einstein, 2007). As explained below, MPT forms the basis of some of the predictions tested in this study.

MPT suggests that different types of PM rely on different processes for success (Einstein et al., 2005; McDaniel & Einstein, 2007). It is theorised that the specific process used depends on the degree of difficulty of the task, with more difficult tasks requiring more strategic effort (McDaniel & Einstein, 2000). For example, a PM task could be based on an event (e.g. return this book to Jane when you see her) or it could be based on time (e.g. return the book to Jane at 5pm). MPT argues that in this instance the event-based task is likely to require fewer cognitive resources. This is because the cue (event) can trigger automatic recall of the intention i.e. seeing Jane will automatically cue the intention to return the book. Conversely, time-based cues may be more difficult and less automatic, i.e.
meeting Jane at 5pm will require increased attention and executive control to monitor for the correct time (McDaniel & Einstein, 2000). However, this is just one feature of PM tasks, and it is important to note that MPT would only lead to the assumption that a time-based task will be more cognitively demanding if the other characteristics of the task are equal. Other characteristics to consider include the length of the delay between intention formation and the execution of the intention, or the focality of the cue in relation to the associated intention (i.e. the relatedness between the intention and associated cue; Cona, Bisiacchi, Sartori, & Scarpazza, 2016; Tierney, Bucks, Weinborn, Hodgson, & Woods, 2016). Although these examples each relate to varying the demand placed on the executive element of the PM task (difficulty of cue detection), tasks can also vary in terms of demand on retrospective memory e.g. remembering multiple tasks at the same time or longer delays between encoding the intention and executing the action (Kidder, Park, Hertzog, & Morrell, 1997). If these other variables are controlled for, it is logical to assume that a time-based task will be more cognitively demanding than a comparable event-based task. This distinction is central to the current research.

**Other Factors that Influence Prospective Memory**

Given the importance of PM for health, quality of life and daily living, especially in older age, there is value in identifying factors that may interfere with successful PM. One of these factors may be sleep quality. There is extensive literature supporting the relationship between aspects of sleep and general cognitive functioning, however, the relationship between sleep and PM specifically is not well understood. This thesis presents a program of research which aimed to investigate possible relationships between sleep and PM. Importantly, some other key variables likely to be influential for PM are also related to
sleep, namely age and depressive symptomology, and these are considered in the present research.

**Prospective Memory and Ageing**

While previous research has established PM to be important in older age, there have been some inconsistencies in the research regarding the presence of age-related changes in PM abilities. Some early studies on PM and ageing did not observe a relationship (Einstein, Gillies, & McDaniel, 1990), while other findings have shown older adults perform less well in PM tasks compared with younger adults (Craik & Bialystok, 2006; West & Craik, 1999; West, Herndon, & Covell, 2003). This variation in findings may relate to the different types of PM that can be measured, with meta-analytic findings suggesting that age-related deficits may be more likely in more difficult PM tasks (Henry, Macleod, Phillips, & Crawford, 2004; Kliegel, Jager, & Phillips, 2008). For example, this would suggest that age-related PM deficits may be more observable in time-based in comparison to event-based tasks, assuming that all other characteristics of the task are equal.

Complicating this relationship is the theorised age-PM “paradox”. This refers to repeated evidence that while older adults may perform less well in controlled settings (e.g. in experimental laboratory-based tasks) they may, paradoxically, have unaffected, or even superior PM abilities in comparison to younger adults in more naturalistic settings i.e. when completing real-world, day-to-day PM tasks (Aberle, Rendell, Rose, McDaniel, & Kliegel, 2010; Schnitzspahn, Kvavilashvili, & Altgassen, 2018). Possible mechanisms of this are that older adults are more motivated, have lower levels of daily activity absorption and/or are better at using compensatory strategies (e.g. reminders or notes). This paradox is an important consideration for research on PM in ageing: while considering factors that
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Influence both lab-based and naturalistic PM performance is valuable, they are likely to be measuring different aspects of PM. The present program of research used a well-validated semi-naturalistic measure of PM (the Memory for Intentions Screening Test; MIST), to balance the requirements of experimental rigor, with generalisability to everyday PM task demands.

Sleep

Introduction to sleep.

Sleep is a fundamental biological function that is essential for physical and psychological health (Dinges & Banks, 2007; Durmer & Dinges, 2005; Walker & Stickgold, 2006). Interrupted sleep is an important and growing public health problem with overwhelming society costs including loss of performance and productivity, dangerous driving, and even mortality and morbidity (Jackson et al., 2016; Sleep Health Foundation, 2018; Wells & Vaughn, 2012). In fact, a recent report from Deloitte estimated that in total, the cost of inadequate sleep in Australia was $66.3 billion in 2016-17 (financial costs and loss of wellbeing; Deloitte, 2017). Therefore, research investigating the effects of sleep is crucial both at an individual and societal level.

This section of the introduction summarises current sleep literature relevant to this thesis, including features of healthy sleep and the relationships between sleep, age, depressive symptoms and cognitive functioning. Also reviewed are factors that may disturb sleep quality as well as methods of assessing sleep. A distinction is drawn between studies that experimentally manipulate sleep (i.e. sleep deprivation) and those that report the effect of naturally occurring habitual sleep on cognition, the latter being of specific relevance to the present research.
What is good sleep quality?

There are varying approaches to characterising sleep quality in research, which can make it difficult to compare findings across studies. Addressing this, a sleep quality consensus panel at the United States National Sleep Foundation (NSF) outlined a set of recommendations for each age group (Hirshkowitz et al., 2015; Ohayon et al., 2017). They endorsed considering overall sleep quantity (total sleep time; TST): agreeing that fewer than 5 hours or more than 9 hours per night is not appropriate for older adults (Hirshkowitz et al., 2015). They also recommended considering measures of sleep quality across three domains: 1) sleep continuity, 2) sleep architecture and 3) daytime naps (Ohayon et al., 2017).

Sleep continuity refers to the patterns of sleep and wake throughout the night (i.e. sleep wake cycling). This includes sleep onset latency (SOL; time taken to fall asleep), sleep efficiency (SE; proportion of time asleep as a function of time in bed), wake after sleep onset (WASO) and number of awakenings of five minutes or longer (Ohayon et al., 2017). For older adults, the NSF recommended ≤30 minutes for both SOL and WASO, equal to or above 85% sleep efficiency, and fewer than three awakenings of five minutes or longer per night (Ohayon et al., 2017).

Sleep architecture refers to the organisation of sleep stages, representing a continuum of relative depth of sleep, i.e., non-rapid eye movement (NREM) sleep stages 1 and 2 (light sleep), NREM sleep stage 3 (deep or slow wave sleep; SWS) and rapid eye movement (REM) sleep (Colten & Altevogt, 2006; Rechtschaffen, 1988). This is illustrated in Figure 1.1. The NSF reached the consensus that it not appropriate for older adults to spend more than 25% of TST in NREM 1 or more than 85% in NREM 2 (Ohayon et al., 2017). While
REM and SWS are thought to be the most restorative stages of sleep, there may be a point beyond which additional time in REM is not beneficial (NSF consensus indicates that above 40% of TST in REM for older adults does not indicate good sleep quality; Ohayon et al., 2017).

Finally, the NSF recommended considering the amount, timing and length of **daytime naps**. This thesis focuses on sleep as it occurs in the main overnight rest period (sleep quantity, continuity and architecture) and it is beyond the scope of this research to also consider naps. However, naps are important for human health and are likely to play an important role in some of the key outcomes discussed in this thesis (Dhand & Sohal, 2006). Therefore, possible avenues for future research encompassing daytime naps is considered in the General Discussion (Chapter 6) of this thesis.

*Figure 1.1. Hypnogram showing the distribution of sleep stages across the night and presents the cyclic structure of sleep. Blue [solid] colour: NREM (stages 1–3), hatched area: REM sleep (Porkka-Heiskanen, Zitting, & Wigren, 2013).*

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Chapter 1: General Introduction

**Interruptions to sleep quality.**

While it is well established that sleep is fundamental to health and wellbeing, it is also well established that sleep problems are common (Sleep Health Foundation, 2018). A recent survey of Australian adults showed that 40% complained of insufficient sleep either daily or several days a week (Adams et al., 2017). There are various ways in which these sleep problems can occur. In some instances, this may reflect an acute, total loss or delay of sleep (e.g. shift work or jetlag). More common, however, is partial sleep restriction (poor quality of sleep or insufficient amount of sleep), which may be either acute or ongoing. Factors that may lead to partial sleep restriction include medications, alcohol and caffeine intake, or other lifestyle factors (Alhola & Polo-Kantola, 2007). Moreover, sleep disorders, e.g. obstructive sleep apnoea (OSA), insomnia or restless leg syndrome are common and often under diagnosed and can have substantial effects on sleep quality (Ram, Seirawan, Kumar, & Clark, 2010).

**Sleep and ageing.**

The likelihood of sleep being disrupted increases with age (Gooneratne & Vitiello, 2014). Firstly, there is a range of self-report literature suggesting that older adults are the most likely to have sleep complaints, with almost half reporting at least one sleep problem (Morphy, Dunn, Lewis, Boardman, & Croft, 2007; Neikrug & Ancoli-Israel, 2010). Studies that have used comprehensive questionnaires (e.g. Pittsburgh Sleep Quality Questionnaire, PSQI) support this, suggesting that advanced ageing is associated with poorer subjective sleep, even in otherwise healthy older adults, and that this can affect quality of life (Buysse et al., 1991; Tal, 2013).
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There is also objective evidence that sleep continuity changes with age. A large meta-analytic study conducted by Ohayon, Carskadon, Guilleminault, and Vitiello (2004) concluded that older adults take longer to fall asleep (SOL), have lower rates of sleep efficiency, are awake more during the night (WASO) and wake more times during the night in comparison with younger adults (Boselli, 1998; Ohayon et al., 2004). Older age is also associated with less overall total sleep time (TST; Ohayon et al., 2004).

Sleep architecture also changes with advancing age. Van Cauter, Leproult, and Plat (2000) examined combined data from several separate studies and found that, at mid-life (36-50 years), the proportion of SWS was markedly lower in comparison to younger adults (15-25 years), although this then appeared to remain stable into older adulthood (71-83 years). They also found that time spent in REM sleep appeared to stay relatively stable throughout midlife, but older adulthood was associated with more WASO and reduced REM sleep (Van Cauter et al., 2000). In support of these observations, meta-analytic findings by Ohayon et al. (2004) suggest that the percentage of SWS and of REM sleep both significantly decrease with age.

These changes to sleep may occur in part because of typical changes to sleep patterns across the lifespan. However, they may also be because of increased rates of illnesses that affect sleep, including some sleep disorders, which are common in Australia. A 2010 report commissioned by the Sleep Health Foundation estimated that 4.7% of Australian adults aged 20 and above were living with obstructive sleep apnoea (OSA), 1.2% with restless leg syndrome and 3% with primary insomnia (Sleep Health Foundation, 2011). Importantly, OSA, insomnia and restless leg syndrome are all more likely to occur in older vs younger adults (Ancoli-Israel, 2009). Specifically, research suggests that up to 5% of older adults meet criteria for clinically significant insomnia, 20% for OSA, and close to 25% for restless
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leg syndrome, all of which can affect subjective sleep quality and objective sleep continuity and sleep architecture (Ohayon et al., 2004; Sforza et al., 2009). For example, obstructions to breathing in OSA typically result in increased arousals overnight (so that a person can restart breathing) which disrupts the sleep cycle and results in less time in SWS and/or REM sleep, (since these phases come after longer periods of sleep). Likewise, the periodic limb movements associated with restless leg syndrome can also result in arousals, again interrupting sleep quality. Similarly, insufficient overall sleep associated with insomnia often leads to less SWS and REM sleep (Backhaus et al., 2006; Y. Li et al., 2016).

The research on sleep appears comprehensively to suggest that sleep quality does decline with age. This is important, as some have proposed that such sleep changes may play a role in age related the cognitive changes often associated with advancing age (Bruce & Aloia, 2006).

Assessing Sleep

Sleep deprivation studies.

Many studies that investigate the influence of sleep on health (including cognitive health) use sleep deprivation paradigms (Alhola & Polo-Kantola, 2007; Doran, Van Dongen, & Dinges, 2001; Drummond et al., 2000). Such studies investigate the next day (or longer) effects of total or partial sleep restriction, or the restriction of one specific sleep stage. This method of research has provided interesting insights into our overall understanding of sleep, and into what can go wrong without sleep. However, a possible pitfall of this method is that outcomes could reflect responses to the stimulus that was used to restrict sleep e.g. the excessive light, noise or movement (Rechtschaffen, 1988).

Moreover, sleep deprivation studies represent an acute change in typical sleeping patterns, which may have different consequences in comparison to longer term but less extreme
sleep disruption. A person who is experiencing chronic poor sleep may have a chance to compensate or adjust to their sleeping patterns. Therefore, given that habitual sleep interruption is the more common occurrence, information provided by deprivation paradigms may be limited in terms of generalisability. An alternative approach is to observe more naturalistic, habitual sleep.

**Habitual sleep: subjective measurements.**

A common approach of assessing habitual sleep is with subjective measures. This can include self or proxy reports on specific questions, on standardised scales (e.g. Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) and/or on sleep diaries (e.g. Carney et al., 2012). Subjective assessment can provide useful information regarding a person’s perceived sleeping patterns and overall quality, is cost effective and easy to administer. However, subjective measures do not have the capacity to measure details of sleep architecture (e.g. sleep stages), and they leave the possibility for self-report bias and inaccuracies in recall (Van Den Berg et al., 2008). An outline of subjective sleep measurements used in this thesis is provided in Chapter 3.

**Habitual sleep: objective measurements.**

**Objective sleep continuity.**

To circumvent the limitations of subjective sleep assessment, many researchers opt to use objective sleep measures. One well-established and widely used example is actigraphy (de Souza et al., 2003; Sadeh, Hauri, Kripke, & Lavie, 1995). Actigraphy records physical activity using small, portable devices typically worn on the wrist. Based on recorded movement, actigraphy output can provide estimates of sleep continuity (specific variables in output vary between device makes and models). These are popular devices in both
clinical and research settings as they are non-intrusive, so can be worn in the participant’s own home (do not require laboratory assessment). They are also relatively cost-effective compared with other methods of objective sleep assessment (discussed below). An outline of sleep assessment using actigraphy is provided in Chapter 4 of this thesis.

**Sleep architecture.**

In comparison to sleep continuity, more comprehensive equipment is required to quantify sleep architecture. As mentioned, sleep architecture refers to the cycling across NREM sleep (stages 1-3) and REM sleep (figure 1.1; Porkka-Heiskanen et al., 2013). Sleep architecture is more difficult to measure, as it cannot be assessed with self-report or activity monitoring. Instead, electroencephalogram (EEG) is required to assess the amplitude of brain waves (figure 1.2; Porkka-Heiskanen et al., 2013).

Overnight polysomnography (PSG) is considered to be the gold standard for assessing sleep, and it can provide detailed, objective information regarding sleep architecture including time spent in each sleep stage. PSG can also provide information about sleep continuity, and may do so with more accuracy than actigraphy as it is based on several factors (breathing patterns, brain activity, and oxygen levels) rather than movement alone (Waldon et al., 2016). However, this method is expensive and time consuming and so only one night of data is usually collected (Van de Water, Holmes, & Hurley, 2011). PSG is also quite an intrusive method of assessment, generally requiring attendance at a sleep lab. Even when done in a person’s own bed (portable PSG) it is unlikely to give an accurate representation of a person’s typical sleep unless multiple nights are collected to allow for a first night effect (i.e. sleep may initially worsen while the person adjusts to the sometimes
invasive equipment). Positively, advances in technology are beginning to allow for the assessment of sleep architecture with less intrusive and more cost-effective methods. Although not as comprehensive as PSG, more basic EEG devices are now available that can be worn in the participant’s own home with minimal intrusion. One example of this is the Zeo, which provides simple information about sleep architecture, as well as estimates of sleep continuity based on brain activity (Shambroom, Fabregas, & Johnstone, 2012). An

*Figure 1.2. Human EEG recording showing the different sleep stages: waking and REM sleep characterized by low-amplitude, high-frequency waves and NREM stage 1 through 3 in the order of decreasing frequency and increasing amplitude of the waves (Porkka-Heiskanen et al., 2013). This image was reproduced with permission from Wiley publishing company.*
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Outline of the Zeo, including its function and validation against PSG, is provided in Chapter 5 of this thesis.

**Sleep and Cognition: Three Possible Pathways.**

Good and poor sleepers are repeatedly shown to differ on a range of cognitive tasks across multiple domains, using a variety of assessment methods (for reviews, see Dinges & Banks, 2007; Waters & Bucks, 2011). The primary domains known to be affected by sleep are attention, retrospective memory and executive functioning (Blackwell, Yaffe, Ancoli-Israel, et al., 2011; Holanda Júnior & Almondes, 2016; Waters & Bucks, 2011).

Given that there are various ways of considering and measuring sleep quality, findings can be mixed depending on features of the study design. Therefore, literature on sleep and cognition is discussed with specific relevance to the sleep measurement used (subjective, objective continuity, and sleep architecture) in Chapters 3, 4 and 5 respectively. Of note, however, in all three categories, there is a paucity of research on the effects of poor sleep on PM.

Despite a wealth of research in the field of sleep and cognition, there is no agreed upon consensus regarding the mechanisms by which this relationship may exist (Waters & Bucks, 2011). Following is a summary of three possible explanations, which are that sleep affects cognition as a result of 1) impoverished daytime vigilance due to fatigue, 2) a direct effect of sleep loss on brain structure and/or function, or 3) a mediating role of depression in the relationship between sleep and cognition – that is sleep may lead to depressive symptoms which, in turn, affect cognition.

**The vigilance hypothesis (state instability).**
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One common theory is that sleep loss induces fatigue, resulting in failures in vigilant attention, which then compromises other areas of cognition (Lim & Dinges, 2008). To investigate this, Doran et al. (2001) repeatedly tested participants who were sleep deprived for 88 hours on a sustained attention psychomotor vigilance task. With increased sleep deprivation, they observed that task performance not only became poorer but also increased in variability. The authors concluded that this was because of state instability i.e. sleep loss interrupted the capacity to maintain consistent alertness and attention (Doran et al., 2001). These findings are important for a range of cognitive tasks: as Lim and Dinges (2008) argue in their review chapter, the ability to carry out any demanding cognitive task relies on the ability to sustain attention to that task (Lim & Dinges, 2008). Consistent with this, the same authors (2010) conducted a meta-analysis of the effects of sleep deprivation on cognition and found that the largest effects were in tests of simple, sustained attention (Lim & Dinges, 2010). However, importantly, the body of the literature supporting this hypothesis is based on sleep deprivation studies. Review of the literature suggests that no studies have looked specifically at habitual sleep and vigilance/sustained attention.

Direct effect of sleep on the brain.

Another theory is that poor sleep directly affects brain structure and/or function, which then affect cognition. An early model suggested that OSA resulted in impaired cognition due to damage to the prefrontal regions of the brain cortex (PFC; Beebe & Gozal, 2002). Subsequent findings using Axial CT scans observed brain injury (specifically left dorsomedial frontal damage) associated with insomnia (Koenigs, Holliday, Solomon, & Grafman, 2010). While these studies focus on clinical samples, other research has found evidence to suggest that sleep loss even in healthy adults results in deficits in cognitive skills dependent on frontal
brain regions i.e. executive functions, constructive thinking skills, and, even, emotional intelligence (Killgore, Grugle, Reichardt, Killcore, & Balkin, 2009; Killgore et al., 2008; Nilsson et al., 2005). This is supported by studies that have used functional magnetic resonance imaging (fMRI) scans to show abnormal activity in the PFC as a result of sleep loss (e.g. Drummond et al., 2000; Drummond, Gillin, & Brown, 2001).

Neurological models have also been proposed to explain the impact of sleep loss on memory. In an fMRI study, Yoo, Hoo, Gujar, Jolesz, and Walker (2007) found evidence of irregularities in the temporal lobes, specifically the hippocampi, during new memory encoding in participants following sleep deprivation, which was then associated with poorer delayed recall. Similarly, Drummond et al. (2001) found reduced temporal lobe activity during a verbal learning task after sleep loss, again using fMRI.

In addition to the above, there is a large amount of research that continues to investigate the effects of compromised sleep on the brain, including in ageing, looking at even more detailed functions, e.g. cortical thinning and white matter degeneration (for summaries, see Nilsson et al., 2005; Porkka-Heiskanen et al., 2013). While it is beyond the scope of this thesis to thoroughly review this literature, overall, this evidence suggests that sleep disruption is likely to have direct effects on the brain, especially the frontal and temporal lobes. It therefore stands to reason that there may be related effects for cognitive domains that rely on these brain regions, i.e. executive functions, memory and learning.

**Sleep, cognition and depressive symptoms.**

Finally, it is possible that symptoms of depression, which are commonly associated with poor sleep, could hinder cognitive performance (Riemann, Berger, & Voderholzer, 2001; Tsuno, Besset, & Ritchie, 2005; Wilson et al., 2002). Sleep and depression are closely
interlinked: several studies have found increased depressive symptoms associated with poor sleep, and this relationship is likely bi-directional (e.g. Armitage, 2007; Bower, Bylsma, Morris, & Rottenberg, 2010; Nebes, Buysse, Halligan, Houck, & Monk, 2009).

Unsurprisingly, then, many common measures of depression include at least one item rating subjective sleep quality (Kroenke, Spitzer, & Williams, 2001). In fact, self-reported changes in sleep patterns is one of the current diagnostic criteria for Major Depressive Disorder in the diagnostic and statistical manual of mental disorders (DSM-5; American Psychiatric Association, 2013). It could be that the presence of depressive symptoms partially explains the relationship between sleep and cognitive performance, given that depression is also a predictor of poorer performance across a range of cognitive domains, (for review, see: Rock, Roiser, Riedel, & Blackwell, 2014).

Of note, this relationship is not exclusive to clinically depressed populations. Many symptoms of depression can occur acutely, without indicating diagnosable depression but still affect cognitive performance (Nadler, Rabi, & Minda, 2010). Therefore, it is important to consider depressive symptoms when assessing cognitive abilities, even in non-depressed individuals.

**Depressive symptoms, Sleep and Prospective Memory**

There is evidence that PM abilities may be affected by symptoms of clinical and sub-clinical depression. Y. R. Li, Weinborn, Loft, and Murray (2013) found that depressed individuals performed less well on PM tasks (measured with the memory for intentions screening test; MIST) compared with non-depressed individuals, but only for more demanding tasks i.e. time-based or long delay). Similarly Y. R. Li, Weinborn, Loft, and Maybery (2014) also found that participants with low reported depressive symptomatology
were able to improve their performance when the importance of the PM task was emphasised, but that this was not the case for those with higher reported depressive symptomatology, despite evidence that both groups increased allocation of attentional resources to the PM task.

**Prospective Memory in Older Adults: is Sleep Important?**

There is an extensive literature on sleep and various aspects of cognition, but there are very few studies that have investigated the relationship between sleep and PM, in any population. There are several ways of investigating this.

Some studies have used experimentally restricted sleep to demonstrate that acute sleep deprivation impairs next day prospective remembering (e.g. Grundgeiger, Bayen, & Horn, 2014). Another variation on this paradigm involves giving a PM intention prior to sleep, to investigate how sleep may affect the consolidation of already encoded PM intentions (e.g. Scullin, 2010). These studies appear to support a link between sleep and PM, however they do not provide insight regarding the effects of more naturally occurring habitual sleeping patterns on day-to-day PM abilities, where sleep occurs prior to both the formation and execution of an intention. This is an important distinction because many daily PM tasks are encoded and completed without the opportunity for a sleep period, but the success with which they are completed may still be influenced by habitual sleep quality. In this thesis, we consider sleep and PM with reference to the relationship between habitual sleep (measured differently in each chapter) and everyday PM, rather than looking at sleep for consolidating encoded PM tasks.

There are a handful of existing studies that have begun to investigate a possible relationship between habitual sleep and PM, both in younger to middle aged adults (Fabbri,
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Tonetti, Martoni, & Natale, 2013, 2015; Kyle et al., 2017) and older adults (Cavuoto et al., 2016). These studies have produced mixed findings, and are reviewed in Chapters 3 and 4 as they apply to subjective and objective sleep. Of note, however, all of these studies have relied on single item tests of PM and have not investigated the effects of sleep on different types of PM processes (e.g., time- vs event-based PM), and they did not investigating possible mechanisms of the relationship between sleep and PM. Therefore, additional research is warranted to further investigate if a relationship exists between habitual sleep and PM in older adults, and to investigate what the possible mechanisms of that relationship may be.

Aims

The aim of this thesis was to build on existing knowledge of sleep and PM and investigate if habitual sleep, measured with multiple approaches assessing subjective and objective sleep continuity and architecture, can predict time-based and/or event-based PM performance in older adults. The primary hypothesis was that cross-sectionally assessed poorer sleep would predict poorer PM performance in our sample of older adults, and that this relationship would be stronger in the more demanding PM subtypes (i.e. time-based rather than event-based tasks). This project also aimed to investigate possible mechanisms of this relationship and explore if other variables known to be important for both sleep and PM (depressive symptoms and other areas of cognition which support PM) may fully or partially mediate this relationship.

Thesis Overview and Organisation

This thesis is comprised of three studies which use the same well-validated measure of PM, but each uses a unique approach to assessing sleep. The following chapter (Chapter 2) outlines the context of each of these three studies and gives specific details about the
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Healthy Ageing Research Program (HARP), this project’s parent research program.

Chapter 3 then describes the first empirical study, which investigated sleep and PM in older adults using subjective measurements of sleep. Chapter 4 builds on these findings and investigates the relationship between PM and objectively measured sleep continuity (actigraphy). Chapter 5 presents the final empirical study, which investigates the relationship between PM in older adults and sleep architecture, specifically time spent in SWS and REM sleep. Each of these three studies assessed PM with a well-validated, semi-naturalistic laboratory-based test of PM, with PM tasks that vary in terms of demand (i.e., both time-based and event-based). Finally, Chapter 6 summarises the findings across studies and presents a general discussion of the implications of results, as well as potential avenues for future research in this field.
Chapter 2: Thesis Context and General Methods
CHAPTER 2

Thesis Context

This chapter describes general methodological details relevant to the parent research program within which the studies reported in this thesis were conducted. It also describes details of research design specific to this thesis.

The Healthy Ageing Research Program (HARP)

All studies in this thesis were conducted within the overarching Healthy Ageing Research Program (HARP). HARP is an observational, longitudinal study, with data collection ongoing since 2009. The program is co-directed by Drs Michael Weinborn and Romola Bucks (MW and RSB; thesis supervisors) and is run within the School of Psychological Science at the University of Western Australia (UWA). The Human Research Ethics Office of UWA has approved all research conducted through HARP (RA/4/1/5361).

HARP Aims and Objectives

The aim of HARP is to investigate age-related change in a variety of cognitive domains in a community dwelling cohort of older adults, and how cognitive changes may be related to everyday functioning. Additionally, HARP examines factors that may influence cognitive changes with age, such as sleep. Although the research centres on typically ageing (non-dementing) older adults, a longer-term aim of HARP is to use our findings to inform treatments and planning for people with cognitive impairments (including dementia), helping them stay independent for longer.

HARP Participant Recruitment
Chapter 2: Thesis Context and General Methods

HARP participants are community volunteers (aged 50+ years) from Perth and regional Western Australia. All participant details are stored in a secure database on the main UWA campus, and participants are invited to return for testing approximately every 18 months. Recruitment for volunteers has involved advertising in community flyers and newsletters and having a HARP presence at community events e.g. Seniors Recreation Council Western Australia (SRCWA) and Have a Go Day. HARP researchers (including the candidate) have also given presentations on topics relevant to ageing (e.g. sleep, cognition, and depression) to local community groups including Men’s Shed, Rotary Clubs and Seniors’ Groups.

**HARP as a Training Opportunity for Students**

The majority of cognitive testing is completed by honours and post-graduate students enrolled in clinical and/or research programs in the School of Psychological Science. Students are fully supervised by program directors and use this testing experience to gain clinical and research experience.

**Community Involvement and Feedback to Participants**

Community volunteers involved in HARP receive a regular newsletter with details of research results, new projects and other up to date information relevant to healthy ageing. All participants are also invited to a bi-annual Open Day, run on the University Campus, which is a rich opportunity for participants to stay involved with HARP research.

**Sleep Research in HARP**

The HARP protocol has always included questionnaires to measure participants’ subjective sleep quality. In 2014, more formal sleep studies were introduced, which allowed for a subset of HARP participants to provide additional information about their
Chapter 2: Thesis Context and General Methods

sleep, complete a comprehensive sleep diary, and wear at-home devices to provide objective estimates of their sleep quality and quantity. Full details regarding the collection of HARP sleep data are outlined in the methods section relevant to each of the three studies in this thesis.

General Method

Participants

The original sample of this study included a total of 278 older adults (50+), who produced 374 unique HARP assessments (92 participated twice and two participated three times). This participation occurred over multiple years of HARP longitudinal data collection, and those who participated multiple times did so at least 15-18 months apart. Specifically, data collected in 2013 and 2014 were included in Study 1, data collected in 2014 and 2015 were included in Study 2, and data collected in 2015 and 2016 were included in Study 3 (see Figure 2.1). Although some assessments were included in more than one study, there were no assessments included in all three studies, and there were no assessments overlapping between Studies 1 and 3. If a participant was tested multiple times in the data collection periods used in one study, their earlier data set was retained ($n = 12$ cases were removed from the data set for this reason). A summary of participant demographics as well as depressive symptoms and general cognitive ability is shown in Table 2.1.

Prior to statistical analysis, the following exclusion criteria were applied for all studies: (i) diagnosis of a major psychiatric disorder (e.g. bipolar disorder); (ii) a history of a significant neurological condition (e.g. stroke); (iii) previous loss of consciousness for more
than 30 minutes; or (iv) probable cognitive impairment (Mini Mental State Examination < 24; Folstein, Folstein, & McHugh, 1975). Participants were also excluded if they had missing data on any of the sleep or cognitive measures relevant to the specific study. All participants were asked if they had a diagnosed sleep disorder and this was recorded.

Summaries of participant demographics for each of the individual studies are presented in the relevant chapters.
Table 2.1. Descriptive statistics on all participants’ demographics, cognition and depressive symptoms (N= 278)

|                          | All participants (N= 278) | Included participants (N= 233) | Excluded participants (N= 45) | Group difference | p =  
|--------------------------|---------------------------|-------------------------------|-------------------------------|------------------|------
|                          | Mean (SD) | Range         | Mean (SD) | Range         | Mean (SD) | Range         |                             |      |
| Age                      | 70.76 (7.33) | 50-93       | 70.55 (7.45) | (50-93)       | 71.84 (6.64) | (57-90)       | .245                         |      |
| % Female                 | 54.4       | N/A          | 65.2       | N/A           | 60         | N/A           | .503                         |      |
| Years of Education       | 13.94 (3.17) | 3-27        | 13.95 (3.12) | 3-27          | 13.85 (3.44) | 7-21           | .850                         |      |
| Time-based PM (MIST), max. 8 | 5.31 (1.39) | 0-8         | 5.36 (1.34) | 0-8           | 4.94 (1.68) | 0-8           | .184                         |      |
| Event-based PM (MIST), max. 8 | 6.68 (1.40) | 0-8         | 6.71 (1.40) | 0-8           | 6.40       | 4-8           | .225                         |      |
| RBANS Total Scale        | 102.43 (13.66) | 70-148      | 103.22 (13.13) | 70-148       | 97.85      | 74-130        | .028*                        |      |
| Retrospective Memory (RBANS) | 102.50 (12.25) | 61-131     | 103 (11.80) | 61-131        | 102 (14.12) | 68-127        | .173                         |      |
| Verbal Fluency (Letter ‘C’) | 16.95 (4.82) | 6-33        | 16.95 (4.82) | 6-33          | 14.20 (4.71) | 4-25          | .061                         |      |
| Verbal Fluency (Actions)  | 18.55 (5.16) | 8-34        | 18.55 (5.16) | 8-34          | 17.10 (4.71) | 6-27          | .078                         |      |
| Working memory/updating (Digits backwards) | 4.74 (1.23) | 2-8         | 4.72 (1.23) | 2-8           | 4.90 (1.22) | 3-8           | .374                         |      |
| Switching (Trails B)      | 78.93 (36.61) | 33-300      | 77.07 (34.55) | 32.57-300    | 89.86 (45.96) | 40-300        | .104                         |      |
| Attention (TEA TS)        | 3.92 (1.12) | 2.15-11.50  | 3.81 (0.92) | 2.15-7.24     | 4.65 (.92)    | 2.53-11.50    | .090                         |      |
| Depressive symptoms (PHQ-9 with sleep item) | 2.67 (3.11) | 0-16        | 2.72 (3.25) | 0-16          | 2.34 (2.26)  | 0-9           | .340                         |      |
| Depressive symptoms (PHQ-8 = PHQ-9 without sleep item) | 1.98 (2.61) | 0-13        | 2.05 (2.76) | 0-13          | 1.59 (1.61)  | 0-7           | .136                         |      |

Note. Sample sizes for each analysis vary depending on available data. MIST = Memory for Intentions Screening test, possible scores range from 1-8, higher scores indicate better performance; RBANS = The Repeatable Battery for the Assessment of Neuropsychological Status, higher scores indicate better performance; Verbal Fluency (C and Actions) = Controlled Oral Word Association, Letter C and Actions tasks, higher scores indicate better performance; Digits backwards = Backwards Digit Span (longest completed string) from the Wechsler Adult Intelligence Scale–Third Edition, higher scores indicate better performance. Trails B = Trails B total seconds, max 300, higher scores indicate poorer performance; TEA TS = Test of Everyday Attention, telephone search task, higher scores indicate poorer performance. PHQ-9= Patient Health Questionnaire- 9, scores of 5 or above (including sleep item) indicate mild depression. Group differences based on chi-squared analysis for categorical variables (gender, sleep disorders) and on independent sample T-tests (equal variances not assumed) for all other variables. *= significant at the .05 level.
Chapter 2: Thesis Context and General Methods

Of the original sample, 45 were excluded ($n = 12$ medical conditions, $n = 22$ missing data on one or more of the measures needed for analysis; more detailed information for reasons for exclusion are provided in individual chapters). The remaining 233 participants had 300 unique assessments (see Figure 2.2). A summary of included participant demographics, depressive symptoms and general cognitive ability, compared with those of excluded participants, is shown in Table 2.1. Average PM performance in this sample was comparable to previous findings in a non-clinical sample of older adults, significantly lower than a sample of healthy younger adults (Woods, Woods, Moran, Dawson, & Carey, 2008) and significantly higher than a sample of older participants with diagnosed mild cognitive impairment (MCI; Karantzoulis, Troyer, & Rich, 2009). Details of these comparisons are presented in table 2.2, and taken together suggest that the participants in the present study demonstrated PM performance consistent with what would be expected in a sample of non-clinical older adults.

Materials

Sleep measures.

In each of the three studies presented in this thesis, a different approach to sleep measurement was used. The first study used self-report data collected with the Pittsburgh sleep Quality Index (PSQI; Buysse et al., 1989). The second used wrist actigraphy (wActiSleep-BT) and the third used Zeo headset devices. Details of each measure is provided in the relevant chapters.

Neuropsychological and depression measures.

The following measures were used across all studies:
Depression. Patient Health Questionnaire 9-item scale (PHQ-9; Kroenke & Spitzer, 2002; Kroenke et al., 2001) was used to assess depressive symptoms, but was modified to remove the sleep-related item (“Trouble falling or staying asleep, or sleeping too much”). The total score was calculated as the sum of the remaining 8 responses (maximum of 24), called PHQ-8 in results. Higher scores indicate more severe depressive symptoms.
Table 2.2. Comparison of MIST scores with previous clinical and non-clinical findings

<table>
<thead>
<tr>
<th>Sample</th>
<th>N</th>
<th>Mean age (years)</th>
<th>PM sub-type (MIST)</th>
<th>PM Score</th>
<th>Hedge’s g (95% CI)</th>
<th>Significantly different from current sample?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy younger adults¹</td>
<td>67</td>
<td>41.2</td>
<td>Time-based</td>
<td>6.7 (1.2)</td>
<td>1.02 (0.75-1.30)*</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Event-Based</td>
<td>7.6 (0.6)</td>
<td>0.71 (0.44 to 0.99)*</td>
<td>Yes</td>
</tr>
<tr>
<td>Healthy older adults²</td>
<td>27</td>
<td>73</td>
<td>Time-based</td>
<td>5.07 (1.6)</td>
<td>-0.17 (-0.57 to 0.23)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Event-Based</td>
<td>6.55 (1.68)</td>
<td>-0.09 (-0.49 to 0.30)</td>
<td>No</td>
</tr>
<tr>
<td>MCI²</td>
<td>27</td>
<td>75.7</td>
<td>Time-based</td>
<td>3.04 (1.7)</td>
<td>-1.60 (-2.01 to -1.18) *</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Event-Based</td>
<td>5.25 (2.0)</td>
<td>-.98 (-1.38 to -0.58) *</td>
<td>Yes</td>
</tr>
</tbody>
</table>


**Prospective Memory (PM).** The Memory for Intentions Screening test (MIST) version adapted for research (Raskin, 2009) is a semi-naturalistic, 8-item, lab-based PM task that takes 30 minutes to complete. The MIST assesses both time-based PM (e.g. in 20 minutes tell me that it’s time to take a break) and event-based PM (e.g. when I give you the red pen, sign your name). Tasks are given with a mix of short and long delays (2 and 15 minutes) and participants are asked to remember and execute the tasks while completing an ongoing task (word search). The MIST has been found to be a valid measure of PM in healthy older adults, with excellent inter-rater reliability (Woods et al., 2008). The MIST can be used to produce subscale scores for both time-based and event-based PM, with possible scores ranging from 0-8 (higher scores indicating better performance).

**Attention.** The Test of Everyday Attention (TEA; McAnespie, 2001) consists of eight sub-tests based on ecologically plausible activities that require attention. As a whole, this has high test-retest reliability, and correlates significantly with other measures of attention.
Chapter 2: Thesis Context and General Methods

(Robertson, Ward, Ridgeway, & Nimmo-Smith, 1996). The present study uses the Telephone Search task subscale of the TEA (TEA-TS), which requires the participant to look through telephone directories and identify symbols while inhibiting similar, but irrelevant, stimuli. Higher scores are awarded for both speed and accuracy. This subtest has been shown to produce significantly different performance in participants with and without traumatic brain injury (Bate, Mathias, & Crawford, 2001), and has been validated in samples of older adults, including very old adults (80+ years: van der Leeuw et al., 2017). Higher scores in this subtest are indicate better performance, and are used as an indicator of attention in all studies in the current thesis.

**Retrospective Memory.** The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) Delayed Memory Index (DMI; Randolph, Tierney, Mohr & Chase, 1998) is calculated based on performance on story memory (free recall), figure memory (free recall) as well as list learning (free recall and recognition), with higher scores indicating better performance.

**Executive Function (EF).** Participants were assessed across multiple EF subdomains (e.g., Fisk & Sharp, 2004). (A) To assess working memory/updating: Backwards Digit Span from the Wechsler Adult Intelligence Scale–Third Edition (WAIS–III; Wechsler, 1997) with higher scores indicating better performance. (B) To assess mental flexibility/shifting: Trail Making (Trails B; Army Individual Test Battery, 1944; Reitan & Wolfson, 1985), higher scores indicating poorer performance. (C) To assess generativity: Controlled Oral Word Association Letter C and Actions (Piatt, Fields, Paolo, & Troster, 1999), with higher scores indicating better performance.
Chapter 2: Thesis Context and General Methods

As there were four variables used to test EF, a Principal Components Analysis (PCA) was conducted to obtain an overall EF measure. All HARP participants tested in 2015 and earlier were included in the PCA (HARP 2016 data was not yet finalised when this factor analysis was conducted). Again, if anyone participated multiple times, only the first case was retained. After removing duplicates, the sample included 333 unique cases. Demographics for participants included in this PCA were broadly similar to those included in the main analysis of the study: they were aged 50 to 90 years (M±SD 70.02±7.46), had an average of 13.6±3.17 years of education and were 64.6% female.

EF variables were assessed for normality and all but one were found to be within acceptable limits based on the criteria outlined by Curran and West (1996). Trails B was found to have moderate positive skew and so was transformed with a square root transformation. No univariate or multivariate outliers were identified (Tabachnick & Fidell, 2013). The Meyer-Okin measure of sampling adequacy was .65, and Bartlett’s test of Sphericity was significant \( X^2(6) = 112.92, p < .001 \). The PCA results indicated the extraction of one component, which accounted for 47.85% of the total variance in test scores. Factor loadings can be seen in Table 2.3.

Using the factor loadings in Table 2.3, an EF component score for each participant in each study was calculated using the regression method in SPSS (the Trails B scores were deflected so that all scores were in the same direction). This score was then saved and used as the objective EF measure in subsequent analyses, with higher scores indicating better performance.
Chapter 2: Thesis Context and General Methods

Table 2.3

Factor Loadings for Principal Components Analysis of Executive Function Test Scores

<table>
<thead>
<tr>
<th>Variable</th>
<th>EF Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Switching (Trails B)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-.68</td>
</tr>
<tr>
<td>Verbal Fluency (C)</td>
<td>.78</td>
</tr>
<tr>
<td>Verbal Fluency (Actions)</td>
<td>.72</td>
</tr>
<tr>
<td>Working Memory/updating (Digits span backwards)</td>
<td>.54</td>
</tr>
</tbody>
</table>

Note. N = 333. Trails B = Trails B total seconds, max 300, higher scores indicate poorer performance. Verbal Fluency (Letter ‘C’ and Actions) = Controlled Oral Word Association Letter ‘C’ and Actions tasks, higher scores indicate better performance; Digit span backwards = Backwards Digit Span from the Wechsler Adult Intelligence Scale–Third Edition, longest string completed correctly, higher scores indicate better performance. <sup>a</sup>Raw scores transformed using square root transformation.

Procedures

Questionnaires.

Prior to attending the session for cognitive assessment, participants completed a comprehensive set of questionnaires which were posted out to them or given to them at a separate appointment. This questionnaire booklet included general demographic information, medical history and current medications. It also included several self-report measures pertaining to depressive symptoms, health (including sleep health), cognition and activities of daily living. The booklet also included four measures which were completed by a proxy (the participant’s partner, friend or adult child). The participants returned the completed questionnaires when they attended cognitive testing. The at-home questionnaire pack did not include the PHQ-9, which was completed in the assessment session with the researcher. This was done in order to capture the presentation at the time of testing and
allow researchers to ensure participant safety (one of the items on the PSQI asks about suicide ideation).

**Sleep assessment.**

The procedures of sleep data collection vary between studies, and so are explained in detail in each relevant chapter.

**Laboratory assessment.**

The cognitive data used in this study were collected as part of the larger HARP testing battery (approx. 3.5 hours). All HARP participants provided written, informed consent and were offered $15 in reimbursement of their travel expenses. Participants who participated in the HARP sleep sub-study were offered an additional $10 honorarium. The Human Research Ethics Office of the University of Western Australia approved this sub-study (no separate code).

**Statistical Analysis.**

Full details of other statistical analyses conducted in Studies 1-3 are presented in their respective chapters.
Chapter 3: Self-reported Sleep in Older Adults: Pathways to Prospective Memory through Depressive Symptoms and Memory for the Past.
 CHAPTER 3

Abstract

Subjective, habitual sleep quality may be important for cognitive abilities in older adults, however there is insufficient current evidence to determine if prospective memory (PM) is affected, which refers to memory for future intentions. This study aimed to investigate this, and to determine if self-reported sleep is related to objectively-measured time-based and/or event-based PM performance. This study also hypothesised that the relationship between subjective sleep and PM may be partially or fully mediated by one or more variables that are important for both subjective sleep and PM abilities (namely depressive symptoms, attention, executive function [EF] and retrospective memory [RM]). To test this, community dwelling older adults ($N = 170$, 50-93 years) completed the Pittsburgh Sleep Quality Index (PSQI), providing subjective information on sleep onset latency (SOL), sleep efficiency (SE), sleep disturbance and sleep duration (total sleep time; TST). They also completed the memory for intentions screening test (MIST) to assess PM, as well as tests of attention, EF and RM. Current depressive symptoms (self-report) were also assessed. Results indicated that poorer sleep (each of the four PSQI variables) predicted greater depressive symptoms which, in turn, predicted poorer PM performance, both time- and event-based. Results also showed that TST predicated time-based PM via RM. No other significant direct or indirect results were observed. These results suggest that self-reported sleep may be related to poorer PM performance via an increase in depressive symptoms, and less consistently, poorer RM. This study contributes to the growing literature on sleep and PM, and highlights the importance of considering indirect effects. Implications and possible areas for future research are discussed.
Chapter 3: Self-reported Sleep and Prospective Memory in Older Adults

Introduction

Poorer subjective sleep quality in older adults is commonly associated with poorer health outcomes including depressive symptoms (Chang et al., 2014) and poorer performance in various cognitive abilities (Potvin et al., 2012; Waller et al., 2016). Subjective sleep may also be important for prospective memory (PM) which is the ability to plan and execute future intentions, but there is very limited current research investigating this. Moreover, consistent with the multiprocess theory (MPT) of PM, it may be that certain types of PM are affected more than others (e.g. time-based tasks may be more affected than the less cognitively demanding event-based tasks), but, to the authors’ knowledge, no research has looked at this. Finally, if subjective sleep and PM are associated, it may be because they are both related to depressive symptoms and/or other areas of cognition (memory for the past, or retrospective memory [RM], executive functions (EF) and attention). Therefore, these variables may fully or partially mediate the relationship. The present study aimed to address these gaps in the literature and investigate if self-reported sleep is associate with PM in older adults, and if so, which types are most affected. It also aimed to explore potential factors that may mediate the relationship between sleep and PM in older adults i.e. depressive symptoms and other cognitive abilities.

Subjective Sleep and Cognition

Subjective sleep quality is a broad term denoting the way that people view their own sleep (i.e. self-report). One obvious advantage of research characterising sleep in this way, is the ease and accessibility with which it can be assessed, as it does not require expensive or intrusive equipment. Another advantage is that self-report sleep tells us about a person’s
experience of their sleep, which may be important for cognitive functioning over and above their actual sleep quality (i.e. a placebo; Draganich & Erdal, 2014).

There appears to be broad evidence that poorer self-reported sleep quality is associated with poorer cognitive functioning in older adults, including global impairment (Potvin et al., 2012; Waller et al., 2016), attention (Saint Martin, Sforza, Barthélémy, Thomas-Anterion, & Roche, 2012), RM (Gamaldo et al., 2017) and EF (Ling et al., 2016). However there have also been several studies that have not observed significant relationships between subjective sleep variables and cognition (Biddle et al., 2017; Cavuoto et al., 2016; Miyata et al., 2013). Additionally, some studies have found that the relationship between subjective sleep quality and cognition may be contingent on other factors, e.g. Sutter, Zöllig, Allemand, and Martin (2012) observed that better subjective sleep was associated with better semantic fluency, reasoning and shifting, but only in participants with high versus low levels of sub-clinical depression.

A challenge with the research in this field is that there are many ways to measure subjective sleep, e.g. by assessing self-reported sleeping habits or the perceived presence of sleep interruptions including self-reported illness, environmental factors or even nightmares (Gamaldo, Allaire, & Whitfield, 2008; Ling et al., 2016; Saint Martin et al., 2012; Sindi et al., 2018). These different approaches can yield different findings and can be difficult to compare. Indeed, in their literature review, Brewster, Miranda, and Rowe (2015) concluded that the research on the association of subjective sleep and cognition in older adults is so mixed that inferences were difficult to draw and more research was needed.

One subjective sleep variable that seems to be the most consistently predictive of cognition is self-reported sleep time (Brewster et al., 2015). Interestingly, research shows
Chapter 3: Self-reported Sleep and Prospective Memory in Older Adults

that too much sleep, as well as not enough, can be problematic for cognition. For example, Blackwell, Yaffe, Ancoli-Israel, et al. (2011) found that older men with long sleep had poorer reaction times and Chen et al. (2016) found that women with either short or long sleep had a higher risk of developing mild cognitive impairment or dementia. In 2016, Lo, Groeger, Cheng, Dijk, and Chee (2016) conducted a systematic review and meta-analysis of self-reported sleep duration and summarised that both short and long sleep were significantly associated with poorer performance across several cognitive domains including working memory and EF, verbal memory, and attention, but not speed of processing.

**Assessing subjective sleep with the PSQI**

One popular, and well validated, way of assessing subjective sleep is with the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989). The PSQI can provide a quick cut point for distinguishing good sleepers from poor sleepers, which is widely used in sleep and cognition research (e.g. Blackwell, Yaffe, Ancoli-Israel, et al., 2011; Wu, Su, Fang, & Chang, 2012). The PSQI can also generate component scores, some of which correspond to the areas of sleep recommended for consideration by the National Sleep Foundation, e.g. sleep duration, sleep latency, sleep disturbances and sleep efficiency (Ohayon et al., 2017). Of note, the PSQI sleep duration subscale assumes that more sleep is better, which, as discussed, is beginning to be refuted. In line with this, the NSF recommends an ideal total sleep duration of 7-8 hours for older adultS, with less than 5 and more than 9 hours not recommended (Hirshkowitz et al., 2015). Therefore, studies using the PSQI sleep duration component need to be cautious if including participants who report sleeping longer than this.
Chapter 3: Self-reported Sleep and Prospective Memory in Older Adults

**Subjective sleep and PM in older adults**

Subjective sleep quality and PM abilities are both likely to decline with advancing age. Moreover, PM abilities may have specific importance for older adults in terms of quality of life and even independent living. Therefore, it is valuable to investigate the potential factors that may influence PM in ageing, which may include subjective sleep (full reviews of this are provided in the general discussion of this thesis, chapter 1).

There have been some preliminary findings investigating subjective sleep and PM in non-clinical older adults, but none that have found evidence for a relationship. For example, a large British study (with approximately 500,000 adults aged 40–69 years) conducted by Kyle et al. (2017), found no association between subjective sleep quality and performance on a single item event-based computer PM task. However, their sleep measure was limited to a two question survey asking 1) “Do you have trouble falling asleep at night or do you wake up in the middle of the night?” and 2) “About how many hours sleep do you get in every 24 hours? (include naps)” (Kyle et al., 2017). Therefore, this study was lacking detail in both their sleep and PM measure, which may have limited findings.

In another study on subjective sleep and PM, Cavuoto et al. (2016) considered self-reported sleep duration as well as an index variable created from multiple measures of the PSQI (specifically sleep disturbance and SOL). They did not find that these subjective sleep measures predicted PM, however they only used a single item PM task that was tested outside of the laboratory (a habitual button pressing task). To the authors’ knowledge, there are no studies that have examined the relationship between responses on a well validated subjective sleep measure (like the PSQI) and performance on a well validated, laboratory tested, multi-item measure of PM in a sample of non-clinical older adults.
Mechanisms of Harm

If subjective sleep does predict PM abilities, then the mechanisms by which this occurs are also of interest. As reviewed in the general introduction of this thesis, there are three leading hypotheses regarding the potential mechanisms of sleep: briefly, these are explained by sleep’s impact on: a) depressive symptoms, b) attention and arousal, c) specific parts of the brain important for cognition, especially frontal and temporal lobes, which may affect EF and RM. These accounts point to the potential roles of depressive symptoms, attention, EF, and RM in sleep-related cognitive disturbances. Some of these factors have been associated with subjective sleep quality (Gamaldo et al., 2017; Ling et al., 2016; Saint Martin et al., 2012) and they have all been shown to be important for PM (Y. R. Li et al., 2014; Y. R. Li et al., 2013; McDaniel & Einstein, 2000). Therefore, it is possible that any of these variables may fully or partially mediate a relationship between subjective sleep quality and PM performance in older adults.

Aims and Hypotheses

The present study aims to investigate if a relationship exists between self-reported sleep quality and lab-based PM performance in a non-clinical sample of older adults. We hypothesised that: H1 a) poorer subjective sleep (longer SOL, poorer sleep efficiency, less total sleep time, and more disturbed sleep) would predict poorer performance on objectively measured PM tasks. In line with MPT, the more demanding tasks would be more sensitive to sleep related deficits (outlined in General Introduction). Therefore, we also hypothesised that, H1b) the relationship between sleep and PM would be strongest in more demanding PM tasks (i.e. time-based rather than event-based tasks). Assuming an association between sleep and PM was observed, we also hypothesised that this relationship
would be wholly or partially mediated by: H2 a) depressive symptoms, b) attention, c) retrospective memory and/or d) executive functioning.

Method

Participants and Procedures

In total, 211 participants (aged 50+) were recruited through the Healthy Ageing Research Project (HARP, directors MW and RSB). As detailed in the General Methods section (Chapter 2), participants were excluded if they reported a diagnosis of a major psychiatric disorder, a history of a significant neurological condition, previous loss of consciousness for more than 30 minutes or probable cognitive impairment (Mini Mental State Examination <24; Folstein et al., 1975). Participants were also excluded if they did not complete any of the cognitive measures or the PSQI.

Materials

Subjective sleep quality. The Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989). The PSQI is a self-report, subjective scale used to assess a person’s sleep quality based on the previous month. The majority of questions are answered using a Likert scale e.g. “how often have you had trouble sleeping because you wake up in the middle of the night or early morning?” on which responses are scored 0-3, with 3 representing the negative extreme (poorest sleep). Responses on the scale are used to generate seven subscales: 1) subjective sleep quality, 2) sleep onset latency (SOL), 3) sleep duration 3) sleep efficiency (SE), 4) sleep disturbance (SD), 5) sleep medication, 6) use of medication and 7) daytime dysfunction (Buysse et al., 1989). The sum of these scores calculates a global sleep score, with a score of 5 or greater indicating overall poor sleep with good test retest reliability $r = 0.87$ (Backhaus, Junghanns, Broocks, Riemann, & Hohagen, 2002). In
all instances, higher scores indicate poorer subjective sleep quality. Of note to this study, the PSQI has been validated for use in older adults, both men and women (Beaudreau et al., 2012; Spira et al., 2011).

Based on recommendations of NSF, this study focussed on sleep duration (total sleep time; TST) and the available subjective estimates of sleep continuity, i.e. SE and SOL. The NSF also recommends considering time in wake after sleep onset (WASO) and number of awakenings over 5 minutes. While the PSQI does not directly estimate these variables, the SD subscale measures the total amount of sleep disturbance the participant experienced, e.g. due to heat, pain or other reasons. Responses to this presumably indicate how much time the participant feels that they spent awake during the night, due to these disturbances. Therefore, the SD scale was used in this study as a subjective proxy for WASO and number of awakenings. Although larger raw scores on some of these variables denote better sleep (i.e. better sleep efficiency), all responses have been transformed into scaled scores, and so higher scores for all sleep measures used in the following analysis denote poorer sleep.

**Depressive symptoms and cognition.**

Full details of the measures used to calculate depressive symptoms and cognition are outlined in the General Methods (Chapter 2). In summary:

*Depressive symptoms* were measured with the Patient Health Questionnaire (PHQ-9; Kroenke & Spitzer, 2002; Kroenke et al., 2001). Participants completed the whole questionnaire, but for the purposes of the regression analysis a version with the sleep item

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1 The scoring of the PSQI assumes that increased total sleep time always denotes better sleep. However, as noted, too much sleep can also be problematic. Inspection of raw data indicated that only 2 of the participants had over the recommended amount of total sleep. Analyses was run with and without these participants, and results were mostly unchanged. Any differing results are presented and discussed below.
removed (referred to as PHQ-8) was used to counteract confounding influence of sleep quality. Higher scores indicate more reported depressive symptoms in the past week.

**Prospective memory** was assessed with the Memory for Intentions Screening Test (MIST), time-based and event-based subscales (possible scores ranging 0-8), higher scores indicating better performance.

**Attention.** (sustained simple attention) was measured using the Test of Everyday Attention (TEA; McAnespie, 2001) Telephone Search task, higher scores indicating poorer performance.

**Retrospective memory** (RM) was assessed using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) Delayed Memory Index (DMI; Randolph, Tierney, Mohr & Chase, 1998). Higher scores indicate better performance.

**Executive function** (EF) was assessed using Backwards Digit Span from the Wechsler Adult Intelligence Scale–Third Edition (WAIS–III; Wechsler, 1997), Trail Making (Trails B; Army Individual Test Battery, 1944; Reitan & Wolfson, 1985), and the Controlled Oral Word Association Letter C and Actions tasks (Piatt et al., 1999). Higher scores in Trails B indicate poorer performance, while the opposite is true for all other cognitive measures. The same indicator loadings derived from the principal components factor analysis (PCA) detailed in the general method were used to produce general EF domain scores for these data. Higher general domain scores indicate better performance.

**Procedure**

**Questionnaire data and cognitive testing.**

As outlined in the General Methods section (Chapter 2), participants were provided with a HARP pre-testing pack approximately one week before attending cognitive assessment at
Chapter 3: Self-reported Sleep and Prospective Memory in Older Adults

the university. This pack included the PSQI, which the participants could complete at home.

**Statistical Analysis.**

Statistical analyses were performed using IBM SPSS Statistics Version 22. Using Hayes & Preacher’s (2014) indirect regression method, eight separate multiple mediation models examined the effect of subjective sleep (TST, SE, SOL and SD) on event- and time-based PM. Depressive symptoms, attention, RM and EF scores were entered together as potential mediators in each model, to examine whether scores on these variables explain some of the relationship between sleep variables and PM. Two covariates were entered into these models for analysis, being education level (measured as self-reported years of education) and age (years). Both age and education level are likely to be important for PM abilities (Henry et al., 2004; Meng & D’Arcy, 2012). Bootstrapped 95% confidence intervals (CI) using 5000 bootstrap samples were calculated (Hayes, 2013). Given that all hypotheses were developed based on previous research, and to reduce the likelihood of a type 2 error, no adjustments were made for multiple comparisons (Rothman, 1990). An alpha of $p < .05$, two-tailed, was used throughout.

**Results**

Eleven participants were excluded due to history of significant neurological conditions (e.g. stroke, epilepsy), mental illness (e.g. schizophrenia) or probable cognitive impairment (Mini Mental State Examination <24; Folstein et al., 1975), and 36 did not complete key assessment measures (sleep or cognition) and so were removed from analysis. The 170 remaining participants were aged 50 to 93 ($M\pm SD$ 70.37±7.55), had an average of 13.93±3.12 years of education and 139 (66%) were female.
Little’s MCAR test indicated that data missing from the PSQI were missing completely at random, $\chi^2 (193) = 200.26$, $p = .345$. The proportion of missing values was small (less than 1%) and so expectation maximisation in SPSS was used to replace them. There were no other missing data. Descriptive statistics of all variables are reported in Table 3.1.

Abnormal subjective sleep (i.e. global PSQI $\geq 5$) was reported by roughly half ($n = 86, 50.59\%$) of the sample. 23 participants (13.53%) endorsed having a diagnosed sleep disorder (insomnia, $n = 1$; restless leg syndrome, $n = 2$; OSA, $n = 7$; not specified, $n = 13^2$). Total scores on the PHQ-9 indicated that the majority of participants (78.82%, $n = 134$), were not depressed, with the remainder meeting criteria suggesting mild (6.30%, $n = 27$), moderate (3.53%, $n = 6$), and moderately severe depression (1.76%, $n = 3$).

There were no high or very high correlations between sleep variables (above .7; Mukaka, 2012) and so there was no concern of multicollinearity: SOL and sleep duration ($r = .24, p = .001$); SOL and sleep efficiency ($r = .38, p < .001$) SOL and self-reported sleep disturbances ($r = .33, p < .001$); sleep duration and sleep efficiency ($r = .61, p < .001$); sleep duration and sleep disturbances ($r = .24, p = .002$); sleep efficiency and sleep disturbances ($r = .19, p = .012$).

**Covariates**

Older age significantly predicted time-based PM (B [standard error] = -0.05 [.01], $p < .001$), but education did not (B [standard error] = 0.01 [.04], $p = .559$). Neither were significantly predictive of event-based PM (age: B [standard error] = -0.04 [.02] $p = .078$; education: B [standard error] = -0.01, [.02], $p = .693$).

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2 In 2013 HARP data collection, participants were not asked to specify which type of sleep disorder they had been diagnosed with.
Table 3.1.

**Descriptive Statistics for all participants (N= 170)**

<table>
<thead>
<tr>
<th></th>
<th>M±SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimum</td>
<td>Maximum</td>
</tr>
<tr>
<td>Global PSQI Score</td>
<td>5.91 (3.58)</td>
<td>0</td>
</tr>
<tr>
<td>PSQI Sleep duration</td>
<td>0.57 (0.81)</td>
<td>0</td>
</tr>
<tr>
<td>PSQI Sleep onset latency</td>
<td>0.99 (0.94)</td>
<td>0</td>
</tr>
<tr>
<td>PSQI Sleep efficiency</td>
<td>0.88 (1.02)</td>
<td>0</td>
</tr>
<tr>
<td>PSQI Sleep disturbance</td>
<td>1.39 (0.60)</td>
<td>0</td>
</tr>
<tr>
<td>Time-based PM (MIST), max. 8</td>
<td>5.34 (1.37)</td>
<td>2</td>
</tr>
<tr>
<td>Event-based PM (MIST), max. 8</td>
<td>6.63 (1.47)</td>
<td>0</td>
</tr>
<tr>
<td>Depressive symptoms (PHQ-9 with sleep item)</td>
<td>2.69 (3.27)</td>
<td>0</td>
</tr>
<tr>
<td>Depressive symptoms (PHQ-8 = PHQ-9 without sleep item)</td>
<td>2.01 (2.77)</td>
<td>0</td>
</tr>
<tr>
<td>Attention (TEA TS)</td>
<td>3.76 (0.87)</td>
<td>2.15</td>
</tr>
<tr>
<td>Retrospective memory (RBANS DMI)</td>
<td>103.22 (11.84)</td>
<td>61.03</td>
</tr>
<tr>
<td>Executive function factor score</td>
<td>23.13 (6.82)</td>
<td>10.33</td>
</tr>
</tbody>
</table>

*Note.* Global PSQI Score = Sum of all component scores on the Sleep Quality Index (PSQI), possible scores 0-21, higher scores indicate poorer sleep; PSQI Sleep duration = Sleep duration component score on the PSQI, possible scores 0-3, higher scores indicate shorter sleep time; PSQI Sleep onset latency = Sleep onset latency component score on the PSQI, possible scores 0-3, higher scores indicate longer time taken to fall asleep; PSQI Sleep efficiency = Sleep efficiency component score on the PSQI, possible scores 0-3, higher scores indicate poorer efficiency; PSQI Sleep disturbance = Sleep disturbance component score on the PSQI, possible scores 0-3, higher scores indicate more disturbances; Time-based PM (MIST) = total score on the time-based subscale of the Memory for Intentions Screening test, possible scores 0-8, higher scores indicate better performance; Event-based PM (MIST) = total score on the event-based subscale of the Memory for Intentions Screening Test, possible scores 0-8, higher scores indicate better performance; PHQ-9=Patient Health Questionnaire- 9 item version (including sleep item), possible scores 0-27, higher scores indicate more reported depressive symptoms, scores of 5 or above indicate mild depression. PHQ-8 = Patient Health Questionnaire 8 item version (sleep item removed), possible scores range from 0-24, higher scores indicate more reported depressive symptoms; TEA TS = Test of Everyday Attention, telephone search task, higher scores indicate better performance; RBANS DMI = The Repeatable Battery for the Assessment of Neuropsychological Status (delayed memory index), higher scores indicate better performance; Executive Function Factor = Component score of four executive function measures: Trails B, Digit span backward, COWA Verbal fluency (C and Actions), higher scores indicate better performance.
Total and Direct Effects between Subjective Sleep Quality (PSQI) and PM Performance (MIST)

The first hypothesis was that there would be a significant total effect between subjective sleep measures and PM. Contrary to this, none of the four sleep variables had significant total effects (Table 3.2, Models 1-4; path c), or direct effects (path c’) on time-based PM. The same was true of event-based PM (Table 3.2, models 5-8; paths c and c’). That is, neither reported TST, SOL, SE nor SD significantly predicted performance on either PM subtype. As no total or direct relationships were observed, no subsequent analysis was conducted to compare the strength of effect of sleep disturbance on PM subtypes.

Subjective Sleep (PSQI) and Time-Based and Event-Based PM (MIST): Mediation Alternatives

The second hypothesis was that depressive symptoms, attention, executive function or retrospective memory may fully or partially mediate the relationship between subjective sleep and PM. Again, due to the absence of significant overall results in Hypothesis 1, mediation analyses as planned for Hypothesis 2 were not examined. Instead, the potential indirect paths between sleep and PM via cognition and depressive symptoms were examined. As Hayes notes (2013), an indirect effect may still be found in the absence of a total effect, depending on the a, b and ab paths that are present. Regarding the relationship between subjective sleep and the previously considered mediators (a paths), higher scores on all 4 PSQI sleep measures (poorer sleep) predicted greater depression (Table 3.2, models 1-8 paths a1). In addition, higher scores on the sleep duration PSQI subscale (less total sleep) significantly predicted poorer retrospective memory abilities (Table 3.2, models 4 and 8, paths a3). There were no other significant relationships observed between any of the
Table 3.2
Subjective Sleep Quality and Prospective Memory via Possible Mediators

<table>
<thead>
<tr>
<th>Model</th>
<th>Predictor</th>
<th>Mediator</th>
<th>DV</th>
<th>$a$</th>
<th>$b$</th>
<th>$ab$</th>
<th>$c$</th>
<th>$c'$</th>
<th>Covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PSQI- Sleep Latency</td>
<td>Depressive Symptoms</td>
<td>Time-Based Prospective Memory</td>
<td>B= 0.80‡</td>
<td>B= -0.09†</td>
<td>B= -0.07*</td>
<td>B= -0.13</td>
<td>B= -0.01</td>
<td>Age, years of education</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Attention</td>
<td></td>
<td>B= - 0.01</td>
<td>B= 0.11</td>
<td></td>
<td>B= -0.001</td>
<td></td>
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<td></td>
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<td>Retrospective Memory</td>
<td></td>
<td>B= -1.01</td>
<td>B= 0.02†</td>
<td>B= -0.02</td>
<td>B= -0.03</td>
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<td></td>
<td></td>
<td>Executive Function</td>
<td></td>
<td>B= - 0.86</td>
<td>B= 0.03†</td>
<td>B= -0.08 to 0.01</td>
<td>B= -0.09 to 0.0004</td>
<td></td>
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<tr>
<td>2</td>
<td>PSQI Sleep efficiency</td>
<td>Depressive Symptoms</td>
<td>Time-Based Prospective Memory</td>
<td>B= 0.83‡</td>
<td>B= -0.09†</td>
<td>B= -0.07*</td>
<td>B= -0.12</td>
<td>B= -0.02</td>
<td>Age, years of education</td>
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<tr>
<td></td>
<td></td>
<td>Attention</td>
<td></td>
<td>B= - 0.05</td>
<td>B= 0.11</td>
<td></td>
<td>B= -0.01</td>
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<tr>
<td></td>
<td>PSQI sleep disturbance</td>
<td>PSQI sleep duration</td>
<td>PSQI Sleep Latency</td>
<td>PSQI Sleep efficiency</td>
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<tr>
<td></td>
<td>Retrospective Memory</td>
<td>B= -0.73</td>
<td>B= -0.02†</td>
<td>B= -1.01</td>
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<tr>
<td></td>
<td>Executive Function</td>
<td>B= -0.15</td>
<td>B= 0.03†</td>
<td>B= -0.04</td>
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<tr>
<td>3</td>
<td>Depressive Symptoms</td>
<td>B= 1.52‡</td>
<td>B= -0.09†</td>
<td>B= -0.13*</td>
<td></td>
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<tr>
<td></td>
<td>Time-Based</td>
<td>B= 0.04</td>
<td>B= 0.11</td>
<td>B= 0.004</td>
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<tr>
<td></td>
<td>Prospective Memory</td>
<td></td>
<td></td>
<td>(-0.05 to -0.01)</td>
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<tr>
<td></td>
<td>Attention</td>
<td></td>
<td></td>
<td>(-0.07 to 0.02)</td>
<td></td>
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<tr>
<td></td>
<td>B= -0.22</td>
<td>B= 0.02</td>
<td></td>
<td>Age, years of education</td>
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<tr>
<td></td>
<td>Retrospective Memory</td>
<td>B= -2.24</td>
<td>B= 0.02†</td>
<td>B= -0.04</td>
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<tr>
<td></td>
<td>Executive Function</td>
<td>B= -0.90</td>
<td>B= 0.03†</td>
<td>B= -0.03</td>
<td></td>
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<tr>
<td>4</td>
<td>Depressive Symptoms</td>
<td>B= 0.78†</td>
<td>B= -0.08†</td>
<td>B= -0.07*</td>
<td></td>
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<tr>
<td></td>
<td>Time-Based</td>
<td>B= -0.10</td>
<td>B= 0.10</td>
<td>(-0.19 to -0.001)</td>
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<td></td>
<td>Prospective Memory</td>
<td></td>
<td></td>
<td>B= -0.01</td>
<td></td>
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<tr>
<td></td>
<td>Attention</td>
<td></td>
<td></td>
<td>(-0.07 to 0.01)</td>
<td></td>
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<tr>
<td></td>
<td>B= -0.21</td>
<td>B= -0.09</td>
<td></td>
<td>Age, years of education</td>
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<tr>
<td></td>
<td>Retrospective Memory</td>
<td>B= -2.32†</td>
<td>B= 0.02</td>
<td>B= -0.04*</td>
<td></td>
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<tr>
<td></td>
<td>Executive Function</td>
<td>B= -0.04</td>
<td>B= 0.03†</td>
<td>B= -0.001</td>
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<tr>
<td>5</td>
<td>Depressive Symptoms</td>
<td>B= 0.80‡</td>
<td>B= -0.12†</td>
<td>B= -0.09*</td>
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<tr>
<td></td>
<td>Event- Based</td>
<td>B= -0.01</td>
<td>B= 0.002</td>
<td>(-0.21 to -0.03)</td>
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<td></td>
<td>Prospective Memory</td>
<td></td>
<td></td>
<td>B= -0.00003</td>
<td></td>
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<tr>
<td></td>
<td>Attention</td>
<td></td>
<td></td>
<td>(-0.03 to 0.02)</td>
<td></td>
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<tr>
<td></td>
<td>B= -0.02</td>
<td>B= 0.11</td>
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<td>Age, years of education</td>
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<td></td>
<td>Retrospective Memory</td>
<td>B= -1.01</td>
<td>B= 0.01</td>
<td>B= -0.01</td>
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<td></td>
<td>Executive Function</td>
<td>B= -0.86</td>
<td>B= 0.03</td>
<td>(-0.10 to 0.004)</td>
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<td>6</td>
<td>Depressive Symptoms</td>
<td>B= 0.83‡</td>
<td>B= -0.11†</td>
<td>B= -0.09*</td>
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<td></td>
<td>Event- Based</td>
<td>B= -0.05</td>
<td>B= -0.001</td>
<td>(-0.22 to -0.02)</td>
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<td></td>
<td>Prospective Memory</td>
<td></td>
<td></td>
<td>B= -0.0001</td>
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<td></td>
<td>Attention</td>
<td></td>
<td></td>
<td>(-0.02 to 0.03)</td>
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<td></td>
<td>B= -0.07</td>
<td>B= 0.04</td>
<td></td>
<td>Age, years of education</td>
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<td></td>
<td>PSQI sleep disturbance</td>
<td>Depressive Symptoms</td>
<td>Event-Based Prospective Memory</td>
<td>B = 1.52†</td>
<td>B = -0.11†</td>
<td>(-0.05 to 0.02)</td>
<td>B = -0.17*</td>
<td>(-0.36 to -0.05)</td>
<td>B = -0.0001</td>
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<tr>
<td>7</td>
<td>PSQI sleep latency</td>
<td>Attention</td>
<td>B = 0.03</td>
<td>B = -0.004</td>
<td></td>
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<tr>
<td></td>
<td>Retrospective Memory</td>
<td>B = -2.24</td>
<td>B = 0.01</td>
<td></td>
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<tr>
<td></td>
<td>Executive Function</td>
<td>B = -0.90</td>
<td>B = 0.02</td>
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</table>

| 8  | PSQI sleep duration   | Depressive Symptoms | Event-Based Prospective Memory | B = 0.78† | B = -0.10† | (-0.22 to -0.01) | B = -0.08* | (-0.04 to 0.05) | B = 0.001 | (-0.12 to 0.01) | B = -0.03 | (-0.14 to 0.01) | B = -0.001 | (-0.05 to 0.03) | B = -0.12 | B = -0.004 | Age, years of education |
|    | Attention              | B = -0.10           | B = -0.01                    |           |           |                 |           |                 |           |                 |           |                 |           |                 |           |           |                        |
|    | Retrospective Memory   | B = -2.32†          | B = 0.01                     |           |           |                 |           |                 |           |                 |           |                 |           |                 |           |           |                        |
|    | Executive Function     | B = -0.04           | B = 0.02                     |           |           |                 |           |                 |           |                 |           |                 |           |                 |           |           |                        |

Note: N = 170. PSQI = Pittsburgh Sleep Quality Index; Sleep latency = sleep onset latency component score on the PSQI; Sleep efficiency = sleep efficiency component score on the PSQI; Sleep disturbance = sleep disturbance component score on the PSQI; Sleep duration = sleep duration component score on the PSQI; Higher PSQI scores indicate poorer sleep; Time-based PM = total score on the time-based subscale of the Memory for Intentions Screening Test (MIST), higher scores indicate better performance; Event-based PM = total score on the event-based subscale of the MIST, higher scores indicate better performance; Depressive symptoms = total scores on the Patient Health Questionnaire 8-item version (sleep item removed), higher scores indicate more reported depressive symptoms; Attention = total scores on the Test of Everyday Attention, telephone search task, higher scores indicate poorer performance; Retrospective Memory = the repeatable battery for the assessment of neuropsychological status, delayed memory index score, higher scores indicate better performance; Executive function = component score of four executive function measures: trails B, digit span backward, COWA verbal fluency (C and Actions), higher scores indicate better performance. DV = dependent variable; 1 = first mediator; 2 = second mediator; 3 = third mediator; 4 = fourth mediator; † = significant at p < .05, ‡ = significant at p < .001; B = effect size; a = path between the predictor and the mediator; b = path between the mediator and outcome variable; ab = indirect path (via the mediator) between the predictor and outcome variable, presented as effect size, B (bootstrapped 95% confidence interval [CI]); c = total effect of the predictor on the outcome variable; c’ = direct effect of the predictor on outcome variable, independent of the pathway through the mediator; * = significant effect as CIs do not cross zero. Where confidence intervals are exactly 0.00, up to 5 decimal places are presented.
subjective sleep measures and measures of cognition (Table 3.2, models 1-3 and 5-7, paths a2 and a4).

With regard to the relationships between the previously hypothesised mediators and PM (b paths), greater depressive symptoms significantly predicted poorer performance on event-based and time-based PM (Table 3.2, Models 1-8, paths b1)\(^3\). Additionally, better EF predicted better time-based PM (Table 3.2, Models 1-4, paths b4) but not event-based PM (Table 3.2, Models 1-4, paths b4)\(^4\). Better RM performance was significantly related to better time-based PM performance in models of sleep continuity (Table 3.2, Models 1-3, paths b4) but not in TST (Table 3.2, Models 4, path b4). RM was not related to event-based PM (Table 3.2, Models 5-8, path b3). Attention was not significantly related to either type of PM performance (Table 3.2, Models 1-8, paths b2).

Finally, regarding indirect effects (ab paths) of sleep on PM, 8 significant indirect relationships were observed between all four measures of subjective sleep and both types of PM (Table 3.2, Models 1-8, path ab1). Specifically, higher PSQI scores (worse sleep), predicted greater depressive symptoms, which in turn predicted poorer PM, both time- and event-based\(^6\). Another significant indirect effect was observed between TST and time-based PM, again via depressive symptoms (Table 3.2, Model 3, path ab3). In this case, longer TST was predictive of better time-based PM performance, via reduced depressive symptoms.

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\(^3\) When analysis was run without participants who endorsed a diagnosed sleep disorder (n = 13), depression no longer significantly predicted event-based PM.

\(^4\) When analysis was re-run with long sleepers removed (n = 2 participants who reported sleeping more than 9 hours per night), EF no longer significantly predicted PM. This is the only significant change in results that occurred as a result of removing these participants, likely due to a reduction in degrees of freedom.

\(^5\) When analysis was re-run without participants who endorsed having a diagnosed sleep disorder, EF no longer significantly predicted PM. This is again likely due to a reduction in degrees of freedom.

\(^6\) When analyses were run without the 13 participants who endorsed sleep disorders, results were unchanged with the exception that self-reported TST no longer significantly predicted event-based PM via depression. Likely because of the lack of relationship between depression and event-based PM in this subset of participants.
Chapter 3: Self-reported Sleep and Prospective Memory in Older Adults

symptoms. This relationship was not present for event-based PM (Table 3.2, Model 7, path ab3). Neither attention nor EF were significant indirect predictors of either PM sub-type (Table 2, Models 1-8, paths ab 2 and 4).

Discussion

This study aimed to investigate the relationship between self-reported sleep and laboratory-tested PM abilities (time-based and event-based) in community dwelling older adults. Contrary to predictions, no significant total or direct relationships between these variables were observed in our sample. This non-significant finding is consistent with other studies that have looked at sleep and PM (Cavuoto et al., 2016; Kyle et al., 2017). However, the present study added several methodological advantages to these studies (e.g. more comprehensive and validated measures of both PM and subjective sleep) and so it had been hypothesised that this study may have observed significant relationships between self-reported sleep and PM where these previous studies did not. However, this was not indicated in our results, which instead supported the previous research and could be taken to suggest that subjective sleep may not be important for PM in older adults, regardless of PM sub-type.

Examination of the time-based and event-based PM scores showed that while there was a range in PM performance (mostly covering all maximum and minimum possible scores), on average our participants did well even in the more challenging time-based PM. This may be one possible explanation for the absence of significant relationships: had the participants found the test more difficult, or shown more variability in performance, we may have been more likely to detect sleep related deficits.
Chapter 3: Self-reported Sleep and Prospective Memory in Older Adults

It is unlikely that the results can be accounted for solely based on the PM measure used, as this null finding was not unique to PM. In general, subjective sleep quality in this sample also did not predict the other cognitive domains assessed (attention, executive functions, and retrospective memory). This is contrary to some previous findings (Gamaldo et al., 2017; Ling et al., 2016; Saint Martin et al., 2012) but is consistent with others (Biddle et al., 2017; Cavuoto et al., 2016). As discussed in the introduction, there is a lack of clarity in this literature, largely because previous studies have used a variety of approaches when considering cognition and particularly subjective sleep. The one exception to this was the significant relationship between shorter sleep duration and poorer retrospective memory, which supports existing literature pointing to a relationship between shorter sleep and cognitive impairment (Benito-León, Louis, & Bermejo-Pareja, 2013; Blackwell, Yaffe, Ancoli-Israel, et al., 2011; Chen et al., 2016; van Oostrom, Nooyens, van Boxtel, & Verschuren, 2018). The fact that this finding was only observed for TST, but not other measures of subjective sleep, also supports the previously made claim that sleep duration is the subjective sleep variable most consistently predictive of cognitive outcomes (Brewster et al., 2015). Importantly, previous research indicates that excessively long sleep is also likely to negatively affect cognition, however as only two of our participants reported long sleep, we could not explore this possibility (analysis run with and without these participants did not significantly change our findings).

The second hypothesis was that the relationship between subjective sleep and PM would be mediated by other factors known to be important for both sleep and PM, i.e. depressive symptoms, attention, RM and EF. However, as there were no direct relationships observed, mediation could not be conducted. Instead we looked at indirect paths (Hayes, 2013).
Chapter 3: Self-reported Sleep and Prospective Memory in Older Adults

Interestingly, this approach produced a consistent finding across all models: poorer sleep (more disturbances, less total sleep, less efficient sleep and more SOL) predicted increased depressive symptoms which, in turn predicted poorer performance on both time-based and event-based PM. These models showed that, after controlling for age and education, depressive symptoms were consistently and significantly related to both subjective sleep (all measures) and PM (both sub-types) which is consistent with previous research (Chang et al., 2014; Y. R. Li et al., 2014). However, as this research is cross sectional, causation cannot be inferred. It could be that depressive symptoms uniquely affect both cognition and sleep, or that poorer cognition affects depressive symptoms. Moreover, as both sleep and depressive symptoms were assessed with self-report, it could be that those with depressive symptoms were more likely to complain of poor sleep due to negative bias. Even if this were the case, however, this remains an interesting finding, as perception of poor sleep, regardless of actual sleep quality, may be important for cognition (Draganich & Erdal, 2014). Despite these reservations, the repeated suggestion of an indirect path via depressive symptoms is an important finding, and it allows us to propose the interesting suggestion that depression may be key in the role between sleep and PM in older adults.

Another, less consistent, indirect effect was observed between total sleep time (TST) and PM via RM. This relationship was observed only with time-based PM, which is likely because RM on its own predicted better time-based but not event-based PM. In the context of MPT, this is logical, suggesting that the more cognitively demanding time-based PM appears to be more susceptible to deficits in RM and inadequate sleep time (McDaniel & Einstein, 2000).
No indirect effects were observed between subjective sleep and PM via the other cognitive measures (EF and attention). As mentioned, EF was not significantly related to any of the sleep measures, which may be why there was no indirect effect via EF. Interestingly, as with RM, EF predicted time-based but not event-based PM, which again appears to support MPT, in that the more challenging time-based task relied more heavily on executive functions (e.g. for participants to stop what they were doing and check the time without prompting). Of note, the measure of attention in this study was not significantly associated with any of the predictor or outcome measures in this study. This is surprising, because attentional capacity should, arguably, be needed for PM and has repeatedly been found to be impacted by poor sleep (Lim & Dinges, 2008, 2010).

A final consideration of these results is the variability in sleep measures. While there were participants with both the minimum and maximum possible score in each of the four components, suggesting adequate range, the average scores were quite low (typically below 1), indicating that this sample reported mostly good sleep. This may also represent, or affect, specific characteristics of our sample, e.g. those who perceive that their sleep is good may have greater capacity to volunteer in research projects. It is also possible that this may result in a group of older adults with higher than usual cognitive reserve, which may result in resilience to sleep-related cognitive changes (Farfel et al., 2013). A full discussion of the implications of this is provided in the General Discussion of this thesis (Chapter 6) as it is relevant to all three studies.

Limitations and Future Research

Importantly, this study is the first to look at subjective sleep and performance on a well-validated, lab-based measure of PM, assessing two types of PM abilities using an 8-item
Chapter 3: Self-reported Sleep and Prospective Memory in Older Adults

rather than a single item task. However, although the PSQI gives good information about perceived sleep, and is well-validated, including in older adults (Buysse et al., 2008; Buysse et al., 1991), it also presents some limitations. The PSQI may not be as accurate in terms of estimating objective sleep and does not highly correlate with other measures of sleep including polysomnography and actigraphy (Buysse et al., 2008; Landry, Best, & Liu-Ambrose, 2015).

Therefore, to build on these findings, future studies should consider using objective measures of sleep, either with PSG or more portable and cost-effective strategies, such as actigraphy. These studies should still use a comprehensive approach to PM assessment, and consider alternate pathways (e.g. via depressive symptoms or other cognitive domains). Beyond assessing this with objective measurements, there are several potential directions for future research, including looking at clinical populations, experimental trials and potentially even sleep intervention paradigms. Details of these possibilities are discussed in subsequent chapters and, in order to avoid repetition, will not be discussed here.

Another important consideration is the possible effect of multiple comparisons. Given that the hypotheses were formed a-priori, the decision was made not to control for multiple comparisons. However, should we have controlled for this, the significant indirect results observed in the second hypothesis would have remained significant. This decision is consistent across all three studies in this thesis and therefore a full discussion on multiple comparisons and of the risk of Type I error is provided in the General Discussion.

Conclusions

Overall, findings of this study did not support the presence of a direct relationship between subjective sleep and PM in older adults, but did point to possible indirect paths,
via depression, and, less consistently, via RM. This provides interesting introductory findings into the potential relationships, and highlights the importance of considering indirect, as well as direct paths. Future studies could build on this, by using objective methods of sleep measurement, which may reveal relationships with these variables that were not found with subjective measurement.
Preface to Chapter 4

The previous chapter in this thesis investigated the relationship between sleep and PM in older adults using a self-report, questionnaire-based method of sleep assessment (the Pittsburgh Sleep Quality Index; sleep onset latency [SOL], sleep efficiency [SE], sleep disturbance and sleep duration subscales). Although this study did not find any overall relationships between these subjective sleep parameters and either event-based or time-based PM, post-hoc analysis suggested indirect effects between subjective sleep (all measures) and PM (both sub-types) via depressive symptoms, as well as an indirect relationship between sleep duration and time-based PM via retrospective memory.

These results provided insight into the possible relationships between sleep and PM, and suggested that it may be important to look at indirect as well as direct relationships. However, as noted in the previous discussion, an approach that relies purely on self-report for sleep quality can be problematic. To build on these findings, another study was needed to look at objective sleep indicators. While objective estimates will not give information about how a person perceives their own sleep (as in Study 1), they are more likely to give an accurate estimate of true sleep patterns.

The next study in this thesis addressed this, exploring objectively measured sleep continuity (SOL, SE and wake after sleep onset; WASO) and total sleep time using actigraphy. It was predicted that, because of the added advantages of this objective approach, a direct relationship with PM would be observed. In light of the findings in the first study, this second study also hypothesised indirect relationships again via depressive symptoms, attention, EF and/or RM.
Chapter 4: Objectively Measured WASO and Sleep Duration Related to Poorer Time-Based Prospective Memory via Symptoms of Depression in Older Adults: an Actigraphic Study.
CHAPTER 4

Abstract

Objectively measured sleep-wake patterns may be important for prospective memory (PM). Firstly, PM relies heavily on other cognitive domains associated with this form of sleep assessment i.e. attention, executive function (EF) and retrospective memory (RM). Secondly, objectively measured poor sleep is commonly associated with depressive symptoms, which also predict poorer PM. This study aimed to investigate if objective sleep continuity and duration were related to event and/or time-based PM performance, and to explore if indirect effects exist via depressive symptoms or RM as found in Study 1, or via attention or EF. Again, as with Study 1, this was investigated in a sample of older adults, as advanced age is associated with changes in both PM and sleep. In total, 133 community-dwelling older adults, aged 50–93, participated in the study by wearing actigraphy devices for approximately one week before completing a lab-based cognitive assessment. Participants also completed the PHQ-9 to assess current depressive symptoms. A series of multiple regression analyses was conducted to test for total, direct and indirect relationships between SOL, WASO and TST and event and time-based PM. Results showed that poorer sleep, characterised by less TST and more WASO, each predicted greater depressive symptoms, which in turn predicted poorer time-based, but not event-based PM performance. No other direct or indirect relationships between objective sleep and PM were observed. This study builds on the findings from Study 1, adds to the growing literature on sleep and PM and demonstrates the potential importance of objectively measured sleep quantity and continuity as well as depressive symptoms in PM abilities.
Chapter 4: Objective Sleep (Actigraphy) and Prospective Memory in Older Adults

Introduction

Habitual sleep continuity and total sleep time (TST) may be important for prospective memory (PM) abilities in older adults, however, there is insufficient research that has investigated this. Sleep continuity refers to patterns of sleep-wake cycles, i.e. sleep onset latency (SOL), wake after sleep onset (WASO), sleep efficiency (SE) and the number of awakenings over 5 minutes. These variables are recommended for consideration in research by the National Sleep Foundation (NSF; Ohayon et al., 2017). While estimates of these variables can be obtained using self-report, as presented in the previous study, it is also important to look at objective assessment of these measures, which are likely to provide greater accuracy and guard against self-report bias (Lauderdale, Knutson, Yan, Liu, & Rathouz, 2008). Importantly, it is not known whether objective measures of sleep continuity and duration can predict PM performance in older adults, or what the mechanisms of this may be. This is relevant as these sleep parameters have been shown to predict a variety of cognitive impairments, including in domains important for PM: i.e. retrospective memory (RM), and executive function (EF) and attention (Doran et al., 2001; Waters & Bucks, 2011). The present study explored this with a design similar to that used in the previous chapter, although with sleep measured objectively using actigraphy. This was investigated with both time- and event-based PM to investigate if they are affected differently, consistent with multiprocess theory (MPT; McDaniel & Einstein, 2000). Regardless of whether a relationship between sleep and PM was observed, we also investigated if there could be indirect effects via depressive symptoms or underlying cognitive deficits in domains that support PM.

Objectively Measured Sleep in Older Adults
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Older adults may be more likely to experience deficits with PM abilities (especially the more demanding subtypes e.g. time-based). They also typically experience interruptions to sleep quality, including measures of TST and sleep continuity. Therefore, if there is a relationship between these variables, it may be specifically relevant for older adults (additional details of this rationale are provided in Chapter 1).

**Objectively Measured Sleep and PM**

Review of the existing literature showed that just three studies have previously looked at PM and objectively measured habitual sleep continuity, all of which used actigraphy: Fabbri et al. (2013) recruited a sample of younger adults and found that poor sleepers performed less well on a PM task than good sleepers. They made this distinction based on the five sleep variables recommended by the NSF (SOL, TST, WASO, sleep efficiency and number of awakenings lasting over 5 minutes). In a retrospective study, Fabbri et al. (2015) compared a sample of insomnia patients with healthy controls (both younger adults). They observed that both groups performed similarly in PM, but, in the insomnia group, objective (actigraphy) sleep efficiency was significantly associated with PM success in the morning but not evening (Fabbri et al., 2015). Cavuoto et al. (2016) recruited a sample of older adults but did not observe an effect of actigraphic sleep quality (SOL, TST and WASO) on PM performance. All three of these studies assessed PM with a habitual button pressing task which was completed throughout the week of sleep assessment (at lights off/wake up time). Critically, as the instruction to press the button was given prior to the sleep study, PM success in these studies at least partly will have been influenced by overnight consolidation of the PM intention, calling into question whether the study design could validly distinguish between the effects of overnight memory consolidation and of habitual sleep on PM abilities. These
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studies are also limited by their use of a single item PM task, measuring event-based but not time-based PM. Finally, because PM was assessed off-site, it is unclear if participants used memory aides (e.g. notes/alarms/reminders) to assist with performance. To the author’s knowledge, there are no studies that have examined the effect of objectively measured habitual sleep continuity on performance on a well validated, laboratory assessed measure of PM that assesses multiple types of PM performance. This study addressed that gap and investigated if PM was predicted by sleep continuity. It may be that this is more important for time-based PM because, in accordance with MPT, this is a more demanding type of PM and so may be more sensitive to sleep-related PM deficits.

Mechanisms of Harm

If these objective sleep measures do influence PM abilities in older adults it is possible that these relationships may operate indirectly, via the effect of sleep on other factors known to be important for PM. Firstly, poor sleep may impact PM via attention, as there is evidence that poor sleep can result in reductions in arousal which impact attention and vigilance (Andreasen, Spliid, Andersen, & Jakobsen, 2010; Doran et al., 2001). Given that PM requires attention and vigilance to monitor the environment for cues, sleep-related attention deficits may result in subsequent PM deficits (McDaniel & Einstein, 2000). Alternatively, PM tasks require retrospective memory (RM) abilities to encode, consolidate, and retrieve the details of the intention, and executive function (EF) to monitor for cues that the task needs to be completed (Zimmermann & Meier, 2006). It is possible that deficits in these domains, which are affected by poor sleep, underlie sleep related PM deficits (Holanda Júnior & Almondes, 2016; Waters & Bucks, 2011). Finally, and as shown in Study 1, Chapter 3, there is a well-established link between PM and depressive
symptoms (e.g. Y. R. Li et al., 2014; Y. R. Li et al., 2013). Given that disruptions to sleep quality have been associated with symptoms of depression (Riemann et al., 2001; Tsuno et al., 2005), sleep may affect PM via an increase in these symptoms. No published studies have looked at the mechanisms of the potential relationship between sleep and PM.

**Aims and Hypotheses**

This study aimed to investigate if habitual sleep continuity and TST, measured objectively using actigraphy in a sample of older adults, would predict performance on a laboratory test of PM, assessing both time-based and event-based performance. We operationalised poorer sleep as i) longer WASO, ii) longer SOL, iii) lower sleep efficiency and iv) shorter TST\(^7\), and hypothesised that these four parameters would significantly predict poorer PM performance. If a relationship were found, we also hypothesised (H1b) that the relationship would be more prominent in time-based PM compared with event-based performance. This study also aimed to investigate indirect relationships, hypothesising that these same measures of sleep would negatively predict PM via (H2a) depressive symptoms, (H2b) attention; (H2c) executive function and/or (H2d) retrospective memory.

**Method**

**Participants**

Participants were 162 community dwelling older adults aged 50+ who took part in the Healthy Ageing Research Project (HARP) at the University of Western Australia (thesis supervisors RSB and MW directors). General exclusion criteria remained the same across

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\(^7\) While the NSF also recommend considering number of awakenings greater than 5 minutes, this variable was not able to be calculated with the type of actigraphy used in this study. This is explained in the method section below.
all studies in this thesis and are outlined in the General Methods (Chapter 2). Participants in this study were also excluded post-hoc if they did not wear the actigraph device or if they had missing data on any of the cognitive measures. All participants were asked if they had a diagnosed sleep disorder and this was recorded.

**Materials**

**Actigraphy.** Actigraph devices are light-weight activity monitors which are widely used to provide estimates of time spent in sleep and wake (de Souza et al., 2003). Participants were invited to wear wActiSleep-BT devices on their non-dominant wrist for approximately one week. They also completed a daily sleep diary which recorded bed and rise times (Carney et al., 2012). All activity data were visually inspected in Actilife version 6, and the bed and rise times were manually entered using diary data. If any diary data were missing, the bed and rise times were manually calculated based on activity, using Society of Behavioural Sleep Medicine (SBSM) guidelines (Ancoli-Israela et al., 2015). Similarly, if visual inspection of activity data indicated a likely discrepancy (of more than 60 minutes) with diary data, they were scored manually. In total, 9.70% of nights were manually scored. Nights were removed if there were not at least 5 minutes of activity data collected prior to bed time (Ancoli-Israela et al., 2015). Once start and end times were finalised, all included nights were scored with the Cole-Kripke algorithm in ActiLife version 6 using 60 second epochs to determine minutes spent in wake/sleep (Cole, Kripke, Gruen, Mullaney, & Gillin, 1992). Only rest periods with at least five hours of data (300 minutes), including wake time, were retained. Participants with fewer than three nights of minimum data requirements were removed from the data set.
Data output provided four of the sleep quality variables recommended by the NSF: WASO, SOL, sleep efficiency and TST (Ohayon et al., 2017). Although an estimate of number of awakenings was provided, the software does not provide an estimate for number of awakenings over 5 minutes, as recommended, and so this measure was not used in this study (Ohayon et al., 2017).

**Depressive symptoms and cognition.**

The same measures of cognition and depressive symptoms were used across all three studies in this thesis. Details of this are available in the General Methods (Chapter 2).

**Procedure**

Participants were provided with actigraph wrist devices and questionnaires at their first appointment. Participants were shown the devices and shown how to use the device (including correct positioning) by a trained researcher. All participants were given an instruction manual for the device, as well as a phone number that they could use to contact researchers while participating in the study. Participants returned the devices when they presented for cognitive testing at the university approximately one week later, after completing the sleep assessment.

**Questionnaire data and cognitive testing.**

Full details of the procedures for collecting questionnaire data and cognitive testing are outlined in the general method section of this thesis.

**Statistical Analysis**

Statistical analyses were performed using IBM SPSS Statistics Version 22. Using Hayes & Preacher’s (2014) indirect regression method, six separate multiple indirect regression models examined the overall (path c), direct (path c’), and indirect (path ab) effects of sleep
quality (SOL, WASO and TST\(^8\)) on event-based and time-based PM. Participant age and years of education were used as covariates in all models, as older age and lower education are associated with poorer cognitive performance (Evans et al., 1993). Scores on attention, RM, EF and depression were entered together as potential indirect variables in each model, to examine whether the impact of poor sleep continuity on PM might operate via depression or other areas of cognition. 95% confidence intervals (CI) using 5000 bootstrap samples were calculated (Hayes & Preacher, 2014). As in study 1, no adjustment was made for multiple comparisons in order to reduce the likelihood of a type 2 error (Rothman, 1990). An alpha of \(p < .05\), two-tailed, was used throughout.

**Results**

Of the original 162 participants, 9 were removed due to medical conditions (\(n = 2\) multiple sclerosis, \(n = 1\) history of epilepsy and stroke, \(n = 2\) bi-polar disorder, \(n = 2\), stroke, \(n = 2\) LOC >30 minutes). A further 7 were removed where actigraphy data were not available (e.g. device not initialised correctly), while the remainder of actigraphy data sets met minimum requirements for inclusion (at least 3 nights of at least 5 hours of data). Participants were also excluded if they did not complete all of the cognitive testing for measures used in this study (\(n = 13\)). The remaining sample consisted of 133 adults aged 50 to 93 years (M±SD 71.44±7.84), 54% female. Participants had an average of 14.02±3.54 years of education, 71 (53.38%) had over 12 years of education (\(n = 38\) completed undergraduate studies, \(n = 23\) completed post graduate studies). 14.29% of participants (\(n = 19\)) indicated mild depressive symptoms and 3.76% (\(n = 5\)) indicated moderate depressive symptoms (based on the PHQ-9). 13 participants reported at least one diagnosed sleep

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\(^8\) Sleep efficiency was not included as a predictor of time-based and event-based PM, for reasons explained below.
disorder ($n = 1$ insomnia; $n = 4$ obstructive sleep apnoea [OSA]; $n = 1$ central sleep apnoea; $n = 3$ restless leg syndrome; $n = 1$ OSA and restless leg syndrome, $n = 3$ not specified). Participants with diagnosed sleep disorders were included in all analyses in order to maintain the variability of sleep quality in the sample.

Actigraphy devices were worn for an average of 7.07±0.53 nights (range 6 to 11). There was a very high negative correlation between sleep efficiency and WASO ($r = -0.96$, $p < 0.001$) and so sleep efficiency was not used as a predictor to avoid multicollinearity (correlations over .9 categorised as "very high", Mukaka, 2012). The correlations for the remaining variables were low (below .5) or negligible (below .3): WASO and SOL ($r = 0.36$, $p < 0.001$); WASO and TST ($r = -0.07$, $p = 0.412$); SOL and TST ($r = 0.01$, $p = 0.872$), and so were all included as indicators of sleep quality in this study (Mukaka, 2012).

Variables were assessed for normality and skew and kurtosis were found to be within acceptable limits (2 and 7 respectively) based on the criteria outlined by Curran and West (1996). Variables were not inspected for outliers as the main analysis was run in conditional process analysis which is robust against variations of normality (Hayes, 2013). Characteristics of participants’ cognitive and depressive symptoms are presented in Table 4.1 and participant sleep characteristics are presented in table 4.2.

The results from the main analysis, which investigated indirect and direct relationships together, are presented in Table 4.3. Investigation of the covariates showed that age

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9 Analyses were run with and without these participants and the main findings were mostly unchanged, with one exception; one previously significant relationship became non-significant, likely due to a reduction in degrees of freedom. This difference in results is identified below.

10 Inspection of descriptive statistics showed that one participant had long sleep (>9 hours) and so analysis involving TST was run with and without this participant. One previously significant result became non-significant, and this is identified and discussed below. All other results were unchanged regardless of whether this participant was included.
Table 4.1
Descriptive statistics on objective sleep (actigraphy), cognition and depressive symptoms (N= 133)

<table>
<thead>
<tr>
<th></th>
<th>M (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time-based PM (MIST), max. 8</td>
<td>5.35 (1.36)</td>
<td>0-8</td>
</tr>
<tr>
<td>Event-based PM (MIST), max. 8</td>
<td>6.99 (1.13)</td>
<td>4-8</td>
</tr>
<tr>
<td>Depressive symptoms (PHQ-9 with sleep item)</td>
<td>2.46 (2.86)</td>
<td>0-13</td>
</tr>
<tr>
<td>Depressive symptoms (PHQ-8 without sleep item)</td>
<td>1.83 (2.42)</td>
<td>0-12</td>
</tr>
<tr>
<td>Attention (TEA TS)</td>
<td>3.88 (0.93)</td>
<td>2.32-7.24</td>
</tr>
<tr>
<td>Retrospective Memory (RBANS DMI)</td>
<td>102.60 (11.95)</td>
<td>60-126</td>
</tr>
<tr>
<td>Executive Function factor score</td>
<td>23.02 (7.43)</td>
<td>6.64 – 49.88</td>
</tr>
</tbody>
</table>

Note. Time-based PM = total score on the time-based prospective memory subscale of the Memory for Intentions Screening Test (MIST), possible scores 0-8, higher scores indicate better performance; Event-based PM = total score on the event-based prospective memory subscale of the MIST, possible scores 0-8, higher scores indicate better performance; PHQ-9 = Patient Health Questionnaire 9-item version (including sleep item), possible scores 0-27, higher scores indicate more reported depressive symptoms, scores of 5 or above indicate mild depression (scored in abnormal range); PHQ-8 = Patient Health Questionnaire 8-item version (sleep item removed), possible scores range from 0-24, higher scores indicate more reported depressive symptoms; TEA TS = Test of Everyday Attention, telephone search task, higher scores indicate better performance; RBANS DMI = The Repeatable Battery for the Assessment of Neuropsychological Status (delayed memory index), higher scores indicate better performance; Executive function factor score = component score of four executive function measures: Trails B, Digit span backward, COWA Verbal fluency (C and Actions), higher scores indicate better performance.

Table 4.2
Descriptive statistics on objective sleep duration and continuity measured with actigraphy (N= 133)

<table>
<thead>
<tr>
<th></th>
<th>M (SD)</th>
<th>Range</th>
<th>Appropriate</th>
<th>Unclear</th>
<th>Inappropriate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actigraphy - SOL (minutes)</td>
<td>4.55 (3.17)</td>
<td>0.00 -16.86</td>
<td>100% (n = 133)</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Actigraphy - WASO (minutes)</td>
<td>41.61 (21.58)</td>
<td>4.57-117.00</td>
<td>30.08% (n=40)</td>
<td>69.92% (n=93)</td>
<td>N/A</td>
</tr>
<tr>
<td>Actigraphy - Sleep Efficiency</td>
<td>90.17 (4.59)</td>
<td>70.41-98.01</td>
<td>87.97% (n =1 17)</td>
<td>9.77% (n = 15)</td>
<td>0.75% (n = 1)</td>
</tr>
<tr>
<td>Actigraphy - Total Sleep Time</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hours</td>
<td>6.89 (.80)</td>
<td>4.68-9.28</td>
<td>32.33% (n =43)</td>
<td>65.41% (n = 87)</td>
<td>2.26% (n = 2 short; n = 1 long)</td>
</tr>
<tr>
<td>Minutes</td>
<td>413.10 (47.78)</td>
<td>280.86 – 556.67</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. NSF= National Sleep Foundation; SOL = average sleep onset latency across all nights measured with actigraphy, NSF consensus ≤30 minutes appropriate, 31-60 minutes unclear, ≥61 minutes inappropriate; WASO = average minutes in wake after sleep onset across all nights measured with actigraphy, NSF recommendation ≤30 minutes appropriate, ≥31 unclear; Sleep efficiency = time spent asleep as a portion of time spent in bed averaged across all nights measured with actigraphy, NSF consensus ≤74% is inappropriate, 75-84% unclear, ≤85% appropriate; Total sleep time = average total time spent asleep across all nights measured with actigraphy, NSF recommendations are between 7 and 8 hours, 5 and 9 hours inclusive; N/A= not applicable as no recommendations are available.
Table 4.3

*Actigraphic Sleep Variables and Prospective Memory: Possible Pathways*

<table>
<thead>
<tr>
<th>Model</th>
<th>Predictor</th>
<th>Mediator</th>
<th>DV</th>
<th>a</th>
<th>b</th>
<th>ab</th>
<th>c</th>
<th>c'</th>
<th>Covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Wake After Sleep Onset</td>
<td>Depressive Symptoms</td>
<td>Time-based PM</td>
<td>B = 0.03‡</td>
<td>B = -0.14†</td>
<td>B = -0.005*</td>
<td>B = -0.003</td>
<td>B = 0.004</td>
<td>Age, years of education.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Attention</td>
<td></td>
<td>B = 0.002</td>
<td>B = -0.14</td>
<td>B = -0.003</td>
<td>(-0.01 to -0.002)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Executive Function</td>
<td></td>
<td>B = -0.01</td>
<td>B = 0.02</td>
<td>B = -0.002</td>
<td>(-0.003 to 0.001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Retrospective Memory</td>
<td></td>
<td>B = -0.09</td>
<td>B = 0.02†</td>
<td>B = -0.002</td>
<td>(-0.002 to 0.002)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Sleep Onset Latency</td>
<td>Depressive Symptoms</td>
<td>Time-based PM</td>
<td>B = 0.08</td>
<td>B = -0.13†</td>
<td>B = -0.01</td>
<td>B = 0.02</td>
<td>B = 0.02</td>
<td>Age, years of education</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Attention</td>
<td></td>
<td>B = -0.02</td>
<td>B = -0.13</td>
<td>B = -0.003</td>
<td>(-0.03 to 0.003)</td>
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<tr>
<td></td>
<td></td>
<td>Executive Function</td>
<td></td>
<td>B = 0.17</td>
<td>B = 0.02</td>
<td>B = 0.004</td>
<td>(-0.002 to 0.02)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Retrospective Memory</td>
<td></td>
<td>B = -0.07</td>
<td>B = 0.02†</td>
<td>B = -0.001</td>
<td>(-0.02 to 0.01)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Total Sleep Time</td>
<td>Depressive Symptoms</td>
<td>Time-based PM</td>
<td>B = -0.01</td>
<td>B = -0.13†</td>
<td>B = 0.001*</td>
<td>B = -0.002</td>
<td>B = -0.003</td>
<td>Age, years of education</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Attention</td>
<td></td>
<td>B = 0.002</td>
<td>B = -0.13</td>
<td>B = -0.002</td>
<td>(-0.0002 to 0.0002)</td>
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<tr>
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<td></td>
<td>Executive Function</td>
<td></td>
<td>B = -0.004</td>
<td>B = 0.02</td>
<td>B = -0.0001</td>
<td>(-0.001 to 0.0002)</td>
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<tr>
<td></td>
<td></td>
<td>Retrospective Memory</td>
<td></td>
<td>B = 0.01</td>
<td>B = 0.02†</td>
<td>B = 0.0003</td>
<td>(-0.001 to 0.001)</td>
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‡ p < .01
† p < .05
* p < .001
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<tr>
<th></th>
<th>Wake After Sleep Onset</th>
<th>Depressive Symptoms</th>
<th>Event-based PM</th>
<th>B = 0.03‡</th>
<th>B = -0.06</th>
<th>B = -0.002</th>
<th>B = 0.001</th>
<th>B = 0.01</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Attention</td>
<td>B = 0.002</td>
<td>B = -0.01</td>
<td>B = 0.00001</td>
<td>B = -0.001</td>
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<td></td>
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<td>Executive Function</td>
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<td>B = 0.01</td>
<td>B = -0.00001</td>
<td>B = -0.002</td>
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<tr>
<td></td>
<td></td>
<td>Retrospective Memory</td>
<td>B = -0.09</td>
<td>B = 0.02†</td>
<td>B = -0.002</td>
<td>(-0.01 to 0.0003)</td>
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<table>
<thead>
<tr>
<th></th>
<th>Sleep Onset Latency</th>
<th>Depressive Symptoms</th>
<th>Event-based PM</th>
<th>B = 0.08</th>
<th>B = -0.05</th>
<th>B = -0.003</th>
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<tr>
<td></td>
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<td>B = -0.01</td>
<td>B = 0.0001</td>
<td>B = 0.02</td>
<td>B = -0.001</td>
<td>B = -0.01</td>
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<tr>
<td></td>
<td></td>
<td>Executive Function</td>
<td>B = 0.17</td>
<td>B = 0.01</td>
<td>B = 0.003</td>
<td>(-0.02 to 0.002)</td>
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<tr>
<td></td>
<td></td>
<td>Retrospective Memory</td>
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<td>B = 0.02†</td>
<td>B = -0.001</td>
<td>(-0.02 to 0.01)</td>
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<table>
<thead>
<tr>
<th></th>
<th>Total Sleep Time</th>
<th>Depressive Symptoms</th>
<th>Event-based PM</th>
<th>B = -0.01</th>
<th>B = -0.06</th>
<th>B = -0.003</th>
<th>B = -0.002</th>
<th>B = -0.002</th>
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<td></td>
<td></td>
<td>Attention</td>
<td>B = 0.002</td>
<td>B = 0.02</td>
<td>B = 0.0002</td>
<td>(-0.004 to 0.001)</td>
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<tr>
<td></td>
<td></td>
<td>Executive Function</td>
<td>B = -0.004</td>
<td>B = 0.01</td>
<td>B = -0.0004</td>
<td>(-0.001 to 0.0004)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Retrospective Memory</td>
<td>B = .01</td>
<td>B = 0.02†</td>
<td>B = 0.0003</td>
<td>(-0.001 to 0.0002)</td>
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</tbody>
</table>

Note. N= 133. Wake after sleep onset = average number of minutes in wake after sleep onset across all nights measured with actigraphy; Sleep onset latency = average number of minutes taken to fall asleep across all nights measured with actigraphy; Total sleep time = average time spent asleep across all nights measured with actigraphy. Time-based PM = total score on the time-based prospective memory subscale of the Memory for Intentions Screening Test (MIST), higher scores indicate better performance; Event-based PM = total score on the event-based prospective memory subscale of the MIST, higher scores indicate better performance; depressive symptoms= score on the Patient Health Questionnaire 8 item version (sleep item removed), higher scores indicate more reported depressive symptoms; Attention = score on Test of Everyday Attention telephone search task, higher scores indicate better performance; Executive function = component score of four executive function measures: Trails B, Digit span backward, COWA Verbal fluency (C and Actions), higher scores indicate better performance; Retrospective Memory = The Repeatable Battery for the Assessment of Neuropsychological Status (delayed memory index), higher scores indicate better performance; DV = dependent variable; † = significant at p < .05, ‡ = significant at p < .001; B = effect size; a = path between the predictor and the mediator; b = path between the mediator and outcome variable; ab = indirect path (via the mediator) between the predictor and outcome variable, presented as effect size, B (bootstrapped 95% confidence interval [CI]); c = total effect of the predictor on the outcome variable; c’ = direct effect of the predictor on outcome variable, independent of the pathway through the mediators; * = significant effect as CIs do not cross zero. Where confidence intervals are exactly 0.00, up to 5 decimal places are presented.
significantly predicted time-based PM, \( B \) [standard error] = -0.05 [0.01], \( p < .001 \), but not event-based PM (\( B \) [standard error] = -0.01 [0.01], \( p = .239 \)). Total number of years of education did not predict either time-based (\( B \) [standard error] = 0.02 [0.03], \( p = .523 \)) or event-based PM based (\( B \) [standard error] = -0.03 [0.03], \( p = .264 \)).

**Direct Relationships between Actigraphic Sleep Parameters and PM (Time- and Event-Based)**

The first hypothesis was that we would observe relationships between sleep (continuity and TST) and PM. To investigate this, each PM subtype was regressed on all three sleep variables controlling for covariates (a total of six models). Neither the total effects of sleep on time-based PM (Table 4.3, model 1-3; paths c), nor event-based PM (Table 4.3, model 4-6; paths c) were significant. That is, minutes in WASO, SOL or TST did not significantly predict performance on either PM subtype. As no total effects were observed, the planned subsequent analyses to compare the strength of total effect of sleep disturbance on PM subtypes (H1b) were not conducted.

**Indirect Effects between Actigraphic Measures of Sleep and PM (Time- and Event-Based)**

The second hypothesis was that we would observe indirect effects between sleep and PM via depressive symptoms or other areas of cognition. The same causal path analyses conducted to test H1 were used to test H2. Inspections of the a paths showed that longer time spent in WASO significantly predicted greater depressive symptoms (Table 4.3, models 1 and 4, path a1). However, this was not the case for the other sleep variables (Table 4.3, models 2, 3, 5 and 6, path a1). Likewise, no sleep variables predicted
performance on any of the cognitive variables: attention, RM or EF (Table 4.3, models 1-6, path a2-4).

Inspection of the b paths indicated that greater depressive symptoms significantly predicted poorer performance on time-based (Table 4.3, model 1-3, path b1) but not event-based PM (Table 4.3, models 4-6, path b1). Better RM performance was significantly related to better event-based and time-based PM performance (Table 4.3, models 1-6, paths b4)\(^\text{11}\), but performance on EF and attention were not significantly related to either type of PM performance (Table 4.3, models 1-6, paths b2 and b3).

Inspection of the ab paths suggested a significant indirect relationship between WASO and time-based PM performance via depressive symptoms (Table 4.3, Model 1, path ab1). Specifically, longer WASO was predictive of poorer time-based PM via greater levels of depression. A second significant indirect effect was observed between TST and time-based PM, again via depressive symptoms (Table 4.3, Model 1, path ab1). In this case, longer TST was predictive of better time-based PM performance, via lower depressive symptoms\(^\text{12}\). No cognitive variables were significant indirect predictors (Table 4.3, Models 1-6, path ab2-4). No indirect effects were observed with SOL or with any sleep variables and event-based PM performance (Table 4.3, Models 2,4,5,6 path ab1).

**Discussion**

This study aimed to investigate the possible relationships between objective measures of sleep (continuity and TST) and PM in community dwelling older adults. Firstly, we hypothesised that there would be a direct relationship between variables of sleep continuity

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\(^\text{11}\) RM was no longer significantly predictive of time-based PM when participants with sleep disorders \(n = 13\) were removed

\(^\text{12}\) This relationship was no longer significant once the one participant with long sleep (>9 hours) was removed.
Chapter 4: Objective Sleep (Actigraphy) and Prospective Memory in Older Adults

and PM. We expected that this relationship may have been stronger with the more
cognitively demanding time-based PM tasks. However, contrary to expectations, no
significant direct relationships were observed between actigraphically measured sleep and
either type of PM. These results suggest that PM was not significantly predicted by
objective sleep quality in this sample.

Although these findings are not consistent with Fabbri et al. (2013), our study was
looking at older adults, rather than younger adults, which is important because PM abilities
and sleep change with age, and so findings may not have the same implications for older
adults. Similarly, our results are not consistent with those of Fabbri et al. (2015). However,
again, the participants in their sample were younger, and the effect was only observed in
individuals with insomnia, a finding unlikely to be generalisable to a healthy population.
Conversely, our results are consistent with those of Cavuoto et al. (2016), who investigated
actigraphically defined sleep in older adults, but used a less comprehensive measure of PM.
The absence of a direct effect is also consistent with findings in Study 1 of this thesis.

We had expected that significant relationships would have been observed in this study,
as objective measures of sleep have generally been found to be important for other
cognitive domains which we know are important for successful PM: namely, attention, RM
and EF (Doran et al., 2001; Holanda Júnior & Almondes, 2016; Waters & Bucks, 2011). It
is possible that PM differs to these domains and is not related to sleep, however this
interpretation would not be supported by the rest of the results. Specifically, sleep was also
not found to be significantly related to attention, EF or RM. This pattern of findings is not
what is typically seen in similar research with adults or older adults (Cavuoto et al., 2016;
Doran et al., 2001; Waters & Bucks, 2011). Therefore, it is more likely that unique
attributes of this sample influenced results, i.e. 1) reduced variability in sleep disturbance, 2) specifics of the cognitive measures, or 3) other characteristics of this sample.

First, inspection of participants’ sleep variables suggests possible insufficient variability. The clear majority (87-100%) of participants fell into the NSF appropriate range for sleep efficiency, SOL and TST. Although one of these participants actually had too much sleep, analysis run without this person did not yield significantly different results. While only just over 30% of participants fell into the optimal range for WASO (less than 30 minutes), it is important to note that the NSF failed to reach a consensus regarding what denotes “inappropriate” WASO for older adults (Ohayon 2017). The recommended 30 minutes is the same for younger adults and, given that the mean WASO in this sample was just over this (approx. 42 minutes), it may be that this recommendation is too stringent. Together, the sleep characteristics suggest that these participants had largely adequate sleep quality, so this may have made it been more difficult to establish a relationship with the cognitive variables, including PM. This may also partly explain why these results differ from Fabbri et al. (2013) who used similar sleep parameters, but directly compared good and poor sleepers.

Alternatively, results may have been limited by other sample characteristics. The participants in this sample had a high average number of years of education, and over half (53.4%) had more than 12 years of formal education. It may be that our participants were not typical of the population, but rather of a more educated sample of older adults, which may have increased their cognitive performance (Roldán-Tapia, Cánovas, León, & García-García, 2017). Of note, Cavuoto et al. (2016), who also did not observe a relationship between sleep and PM reported a similar education rate, with 55.5% having more than 12
Chapter 4: Objective Sleep (Actigraphy) and Prospective Memory in Older Adults

years. Fabbri et al. (2015), who did observe a difference between groups on PM performance did not report the overall education level of their sample. However, results indicated that education did not have a significant relationship with either of the PM measures in this sample. As mentioned in the previous study, it may be that the high education levels in our sample increased resilience against sleep- or age-related cognitive decline (i.e. cognitive reserve; Farfel et al., 2013) and this is discussed in Chapter 6.

The second aim of this study was to explore possible indirect relationships between sleep and PM via either attention, RM, EF, and/or depressive symptoms. Results showed that longer WASO was significantly associated with more self-reported depressive symptoms which, in turn, significantly predicted poorer performance on time-based PM. Similarly, a significant indirect effect was observed between longer TST and better time-based PM, again via greater depressive symptoms. These findings, which were not accounted for by age or education, suggest that when taken together, sleep (WASO or TST) and depressive symptoms can predict older adults’ PM abilities in more demanding PM tasks. Such findings also speak against the idea that restriction of range in sleep or PM ability can account for the lack of an overall relationship. This indirect effect is consistent with previous research that has repeatedly demonstrated depressive symptoms as being related to both poorer sleep quality and PM performance (Y. R. Li et al., 2014; Y. R. Li et al., 2013; Riemann et al., 2001; Tsuno et al., 2005). Importantly, these indirect relationships were not found for event-based PM. Consistent with MPT, it is possible that this reflects the increased level of strategic demand required for time-based tasks, which in turn may have been more sensitive to subtle deficits caused by relatively mild sleep and depressive...
symptoms. Participants may have been more able to overcome these challenges with the less demanding PM tasks.

As already discussed, sleep did not significantly predict performance on any of the cognitive variables measured in this study, and so, unsurprisingly, no significant indirect relationships were observed via attention, RM or EF. To explore this further however, relationships between PM and these other cognitive variables were considered. Of note, EF and attention performance were not significantly related to PM performance, either time-based or event-based. This is in contrast to expectations, as previous research has indicated that executive attentional control is important for monitoring the environment and detecting cues that a PM intention needs to be executed (McDaniel & Einstein, 2000).

As expected, better performance on RM predicted better PM performance, both time-based and event-based. This is unsurprising, given that RM is essential for remembering the details of the PM task that needs to be completed, and is consistent with previous research indicating that RM is integral for successful prospective remembering (Zimmermann & Meier, 2006). Therefore, the absence of a significant indirect effect between sleep and PM via RM seems to be a reflection of the lack of an overall relationship between sleep and cognition in this study.

This study considered three of the sleep continuity measures recommended by the NSF. The Foundation also recommends considering the number of awakenings longer than five minutes, however this measure was not available with the software used in this study, which only provided a count of all awakenings, regardless of length. The five-minute cut-off is most likely recommended to guard against including short or micro awakenings, which may be less likely to significantly interrupt sleep architecture. Therefore, including
shorter awakenings could result in an overestimation of sleep disruption. The Cole-Kripke algorithm used in this study was based on 60 second epochs; and so even without a specified cut off, no awakenings under one minute would be registered. Theoretically, it is unclear if a wake period of one to four minutes would affect sleep architecture in a significantly different way to a wake period of five minutes. It is therefore possible that considering number of awakenings with no specified time limit may still have provided useful information in this study, and this could be considered in future research.

The study design had several notable strengths: it used a non-obtrusive, evidence based and widely used form of sleep equipment, which gave an objective estimate of multiple sleep quality measures recommended for use by the NSF. The study also used a well-established, evidence-based measure of PM, which assessed multiple types of PM performance and offered more in-depth information regarding PM abilities than would be possible using single item tasks (e.g. Cavuoto et al., 2016; Fabbri et al., 2013). Moreover, PM was assessed in the laboratory by trained researchers, which controlled against the influence of memory consolidation during sleep and did not allow for memory assisting techniques (e.g. setting reminders), which can influence PM success. This study is also unique in that it assessed several other possible factors, known to be important for both sleep and PM, which could have influenced the overall relationships.

As the current research is cross-sectional, results cannot be used to infer causation. While it is possible that poorer sleep increased depressive symptoms, which led to poorer PM, the directions of these effects are unclear. To add to the findings of this study, future research may consider longitudinal examination of these sleep parameters and cognition, which would give information about causation.
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Future research could also consider using alternative measures of objective sleep, which could measure different aspects of sleep quality. Although actigraphy is well validated and has several practical strengths, it cannot provide information on sleep architecture or estimate time spent in different sleep stages, variables also recommended for consideration by the NSF (Ohayon et al., 2017). Moreover, actigraphy classifies wake time based on physical activity alone, which may miss some wake periods if there is limited movement, possibly especially so in older adults who have less movement. Supporting this, Sivertsen et al. (2006) found that actigraphy performed poorly in detecting wakefulness in comparison to PSG in a sample of older adults. It is possible, then, that this approach results in an underestimation of sleep disturbance and could have reduced the variability in sleep measures in this sample. Findings from J. L. Martin and Hakim (2011) indicate that this may specifically limit the validity of the estimation of SOL estimated with actigraphy, which may explain why this was the only sleep parameter that did not yield a significant indirect effect with PM. To address these questions, future research could use electroencephalogram (EEG) to establish wake/sleep patterns, and identify different sleep stages.

The findings of this study do not support an overall relationship between objective sleep and PM performance in older adults. However, they do indicate an indirect relationship between both WASO and TST with time-based PM, via self-reported depressive symptoms. These findings may have implications for interventions and could suggest that PM abilities could improve with improved sleep and/or depressive symptoms.
Preface to Chapter 5

The previous two studies in this thesis investigated the relationship between habitual sleep and lab-based prospective memory (PM) in older adults. A strength of the research thus far is that sleep has been assessed comprehensively with both subjective (questionnaire) and objective (actigraphy) measures. Interestingly, similar findings were observed in both studies, suggesting indirect relationships between sleep and PM, most consistently via depressive symptoms.

Importantly, the sleep data presented in these two studies cannot provide information about participants’ sleep architecture, i.e. was total sleep time spent in light sleep, or the more restorative rapid eye movement (REM) or slow wave sleep (SWS)? This is important, because REM and SWS are thought to be the most important for brain health and memory. Moreover, actigraphy codes sleep/wake patterns based on physical movement, which can lack sensitivity (e.g. if the participant is awake but lying still). To build on these first two studies, then, research using electroencephalogram (EEG) could a) provide information about sleep architecture, including time spent in REM and SWS and b) provide potentially more accurate estimates of SOL and WASO.

To address this, the final study in this thesis used the Zeo, a portable single electrode sleep monitoring device, to investigate the relationship between PM and habitual sleep architecture (time spent in WASO and REM) and sleep continuity. Given the findings of the previous two chapters, the study hypothesised that indirect effects would again be observed, but also investigated potential total effects between PM and sleep using these measures, as measuring sleep with EEG may have yielded different results.
Chapter 5: SWS and Sleep Continuity, but not REM Sleep, are associated with Time-Based Prospective Memory via Symptoms of Depression in Older Adults: Using the Zeo to Assess Habitual Sleep Architecture
Chapter 4: Objective Sleep (Actigraphy) and Prospective Memory in Older Adults

CHAPTER 5

Abstract

Habitual sleep architecture, specifically time spent in rapid eye movement (REM) and slow wave sleep (SWS) may be important for prospective memory (PM) abilities in older adults, but there is no existing research that has tested this. This is an oversight in the literature, as both REM and SWS have been associated with other cognitive domains that are important for PM (i.e. attention, executive function [EF] and retrospective memory [RM]). Moreover, changes in sleep architecture and changes in PM are both associated with depressive symptoms. If there is a relationship between REM, SWS and PM, the relationships would likely be observed in older adults, who typically spend less time in these sleep stages, and have poorer PM abilities. The aim of this study was to investigate if habitual time spent in REM and SWS predicted time-based and event-based PM performance in community-dwelling older adults, either directly or indirectly. To assess this, participants wore a portable wireless electroencephalogram (EEG) system on a headband overnight (Zeo device). In total, 103 participants aged 56-86 wore devices at home (3-10, $M = 5.74$ nights) before attending the laboratory for assessment of cognition, including PM. Self-report measures of current depressive symptoms were also assessed. The Zeo can also provide estimates of EEG defined sleep continuity (e.g. SOL and WASO), and so this study also investigated the possible relationships between PM and these variables. Multiple regression analyses were used to test for total, direct and indirect relationships between PM and the EEG-defined sleep variables. Results suggested that SWS, WASO, and SOL, but not REM sleep, predicted poorer time-based PM via increased depressive symptoms. No other direct or indirect relationships were observed.
Introduction

Sleep quality measured with electroencephalogram (EEG) can provide important information not available with other forms of sleep assessment e.g. self-report or physical activity monitors like actigraphy. While these latter measures can estimate sleep/wake cycles and total sleep time (TST), an EEG approach provides information regarding sleep architecture, i.e. the cycling of sleep between light sleep, rapid eye movement (REM) sleep, and slow wave sleep (SWS). With this, time spent in each stage can be calculated, both as an absolute value and as a proportion of TST. This approach, like actigraphy, can also estimate sleep continuity measures, but does so based on brain activity which may be more accurate (J. L. Martin & Hakim, 2011; Rocknathan et al., 2017). Further, time spent in the most restorative sleep stages, i.e. REM and SWS sleep, is likely to be uniquely important for reduced depressive symptoms and improved performance in some cognitive domains (Scullin & Bliwise, 2015a; Steiger & Kimura, 2010; Walker, 2009). Of note to the current research, no published studies have investigated the link between EEG defined sleep and prospective memory (PM) in any age group. This may be of particular relevance to older adults, as PM abilities, and sleep architecture, both change with advancing age (Ohayon et al., 2004). The present study investigated if EEG defined time in REM, time in SWS and sleep continuity could predict PM performance in community-dwelling older adults. As in the previous studies in this thesis, this study also investigated if these relationships operate indirectly via other factors known to be influenced by sleep and important for PM, e.g. depressive symptoms or other areas of cognition.

Sleep Architecture and Cognition
Sleep architecture is important for cognition (Ohayon et al., 2017). Specifically, time spent in REM sleep has been associated with abilities in a variety of cognitive domains in both cross sectional and in longitudinal research (Scullin & Bliwise, 2015a). In a study using one night of laboratory polysomnography (PSG) with middle-aged and older adults, Lafortune et al. (2014) found that more REM sleep was associated with better verbal learning potential. Similarly, Scullin et al. (2015) found that a greater proportion of TST spent in REM significantly correlated with better next day immediate recall, but not with delayed recall or executive function. This study also used one night of PSG data (following an adjustment night), however they investigated this in a clinical sample of participants with Parkinson’s disease. Two PSG studies using large samples of community-dwelling older men found that those participants with a lower percentage of TST spent in REM showed poorer overall cognition (MMSE) and executive function (Blackwell, Yaffe, Ancoli-Israel, et al., 2011; Song et al., 2015). More recently, Della Monica, Johnsen, Atzori, Groeger, and Dijk (2018) found that less time spent in REM (from PSG) predicted lower accuracy across several cognitive tasks the next day, including one of executive function (goal neglect). With relevance to prospective memory, a recent study by Scullin et al. (2019) observed that in a sample of adults (18-84 years), a significant relationship between advanced age and poorer PM consolidation was significantly mediated by less time spent in REM sleep.

Time spent in SWS is also likely to be important for cognition, although this is less well established in cognitive ageing research. Walker (2009) argued that SWS is important not only for the consolidation process, but is also vital before new learning is possible. This is due to the role of SWS in transferring old memories from the hippocampi to the neocortex,
increasing hippocampal-encoding ability the following day. While Walker was referring to the acute effects of SWS deprivation, it would follow that habitually poor SWS may result in chronic cognitive impairment. However, we have not been able to find any studies specifically investigating this.

SWS is also important for prefrontal cortex functioning, suggesting possible implications for complex attention and executive functioning (Wilckens, Erickson, & Wheeler, 2012). Consistent with this, there appears to be an association between SWS and better sustained attention and processing speed across age groups including in older adults in studies of selective SWS deprivation (Ferrara, De Gennaro, Casagrande, & Bertini, 2000; Groeger, Stanley, Deacon, & Dijk, 2014) as well as habitual SWS duration (Della Monica et al., 2018; Edinger, Glenn, Bastian, & Marsh, 2000). Conversely, however, observational studies using PSG have failed to support a link between SWS (proportion) and executive function as measured by the Trail Making task, Part B, approximately one week later (Blackwell, Yaffe, Ancoli-Israel, et al., 2011; Song et al., 2015).

The findings summarised above present SWS and REM as a mixture of 1) absolute duration and 2) time as a proportion of TST. While both approaches are commonly used in the literature, using a proportional value may understate some differences between participants. For example, two participants with 90 and 120 minutes of REM respectively could both spend 25% of their sleep in REM, depending on their TST, (e.g. 360 and 480 mins, respectively) even though the additional half hour of REM could have benefits for the second participant. Moreover, SOL and WASO are not typically presented as percentages, therefore studies that use both types of parameters (such as the current study) would lack
consistency if REM/SWS were presented as proportions. Accordingly, this study uses time spent in REM, SWS, TST and SOL in minutes.

**Sleep Architecture, PM and Older Age**

As previously noted in this thesis, both PM abilities and sleep architecture change with age (full reviews in Chapter 1, General Introduction). Given that sleep architecture is associated with a range of cognitive abilities, including abilities important for PM (attention, RM and EF), it may be that habitual sleep architecture is also important for PM. Importantly, if habitual sleep architecture does predict PM abilities, multiprocess theory (MPT) suggests that this may be especially true for the more demanding PM tasks (e.g. time-based vs event-based tasks) that are most affected by sleep architecture. To the author’s knowledge, there are no studies that have investigated the role of habitual sleep architecture in PM function in older age.

**Mechanisms of Harm**

While it seems likely that sleep architecture and PM in older adults are associated, it is unclear if there is an overall effect, or if these relationships operate indirectly via other factors important for both. The previous findings in this thesis point to an indirect relationship via depressive symptoms, and it may be that these same indirect patterns are observed, again, with EEG-defined sleep architecture. Alternatively, the other two leading hypotheses regarding sleep and cognition point to sleep’s impact on attentional control, or on parts of the brain important for RM and EF. Given that the literature above suggests that sleep architecture may be important for attention, RM and possibly EF, indirect effects could possibly be observed between sleep architecture and PM via these cognitive variables.

**Aims and Hypotheses**
This study aimed to investigate time spent in REM and SWS as predictors of performance on a laboratory test of PM, assessing both time-based and event-based performance in older adults. However, given that this method of sleep assessment can also assess continuity, possibly with greater accuracy than actigraphy, this study also explored SOL and WASO as predictors of PM. We hypothesised that (H1a) better sleep, measured as more REM, SWS and less SOL and WASO, would predict better PM and that (H1b) this relationship would be more prominent for time-based PM compared with event-based performance due to the greater strategic demands inherent in time-based PM. In light of the previous two studies presented in this thesis, this study also investigated potential indirect relationships between sleep and PM, expecting that better sleep may predict better PM (both event and time-based) via (H2a) depressive symptoms (H2b), attention, (H2c) executive function and/or (H2d) retrospective memory.

Method

Participants

Participants were 160 community-dwelling older adults aged 50+ years who participated in the Healthy Ageing Research Program (HARP) at the University of Western Australia (Directors RSB and MW). Details of participant recruitment and exclusion criteria are outlined in the General Introduction of this thesis and are the same as in the previous 2 studies.

Materials

Zeo. A wireless, dry-fabric headband worn overnight to monitor sleep (Zeo Inc. Zeo Newton, MA, USA), the Zeo uses electrophysiological signals from the forehead (approximately Fp1-Fp2) with a single bi-polar channel. The signals are transmitted
wirelessly to a base station, in which an automated algorithm codes sleep stages (wake, NREM, SWS and REM sleep) for each 30 second epoch (Shambroom et al., 2012). The final data for each rest period indicates time spent in each sleep stage and allows for the calculation of total sleep time, SOL and WASO (Shambroom et al., 2012). Sleep/wake classification has been validated against wrist actigraphy with results suggesting reliable use (Tonetti et al., 2013). The Zeo has also been found to have adequate consistency with overnight polysomnography (PSG): using this method of validation, the Zeo could classify sleep/wake states with over 90% accuracy, and could distinguish between sleep stages with approximately 75% accuracy (Shambroom et al., 2012). This device is low cost, portable, and the bands are fully adjustable so that the individual can fit it to their own head. As with Study 2, participants who did not have at least 3 nights of at least 5 hours (300 minutes) of data were excluded from analyses. This study used four sleep variables calculated with the Zeo: average minutes spent in REM per night and average minutes spent in SWS per night (more minutes indicating better sleep)\textsuperscript{13} as well as SOL and WASO (fewer minutes indicating better sleep).

**Depressive symptoms and Cognition.** These measures were unchanged from previous studies in this thesis.

**Procedure**

Participants were provided with Zeo headset devices and questionnaires at their first appointment which occurred either at the university, at another research testing site, or in

\textsuperscript{13} As stated in the introduction of this chapter, we argue that total time spent is likely to be more informative than the proportion of TST. However, for the sake of consistency with previous research, the models involving REM and SWS were re-run calculated as a proportion of TST. This did not yield any significantly different results for analyses involving REM. For analyses involving SWS, two previously significant results became non-significant. These differences are presented and discussed below.
the participant’s home. Participants were asked to wear the Zeo devices at home following their first appointment until attending the university to return the sleep equipment and participate in cognitive testing (typically a week, up to 10 days).

Full details of the procedures for collecting questionnaire data and cognitive testing are outlined in the General Method (Chapter 2).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics Version 22. Using Hayes & Preacher’s (2014) indirect regression method, eight separate conditional process analysis models examined the overall (path c), direct (path c’) and indirect (path ab) effects of sleep quality (SWS, REM, SOL, WASO) on event-based and time-based PM. Participant age and years of education were used as covariates in all models, as these factors are known to influence cognitive performance (Evans et al., 1993). Scores on attention, RM, EF and depression were entered together as potential variables for indirect effects between the predictor and outcome variables. Bootstrapped 95% confidence intervals (CI) using 5000 bootstrap samples were calculated (Hayes & Preacher, 2014). As in the previous studies, no adjustments were made for multiple comparisons (Rothman, 1990). An alpha of $p < .05$, two-tailed, was used throughout.

Results

Of the original 159 participants, one was excluded due to an MMSE total score under 24, seven were excluded due to medical history ($n = 1$ stroke, $n = 1$ multiple sclerosis, $n = 1$ epilepsy, $n = 1$ bi-polar and $n = 3$ participants reported a previous loss of consciousness over 30 minutes). All participants received a Zeo device to take home, however, downloaded data from 35 participants did not meet the minimum requirements (at least 3 nights of 5+...
hours of data) and so were removed. Reasons include: participant did not wear the devices for enough of the study (e.g. due to discomfort), lost signals during the night (e.g. due to movement or sweat), faults in the device used (e.g. battery failure). A further 12 participants were removed due to missing cognitive data and one did not complete the questionnaire measure for depressive symptoms. The remaining 103 participants were aged between 56 and 86 (M±SD 71.06±6.69) and 65 (62.5%) were female; 86 (82.69%) participants had completed over 12 years of education (n = 24 completed undergraduate studies, n = 17 post graduate studies). 14 participants reported at least one diagnosed sleep disorder (n = 1 insomnia; n = 3 obstructive sleep apnoea; n = 2 restless leg syndrome; n = 1 insomnia and restless leg syndrome, n = 7 not specified) but were included in all analyses in order to maintain the variability of sleep quality in the sample\(^\text{14}\). Scores on the PHQ-9 indicated that six participants (5.83%) had moderately severe depressive symptoms, 14 (13.59%) had mild depressive symptoms and the remainder had no or sub-clinical depressive symptoms.

Variables were assessed for normality and all were found to be within acceptable limits. Although some univariate outliers were present, they were retained in the data set as the analysis in this study uses bootstrapping and is robust against outliers and violations of normality (Hayes, 2013). Descriptive statistics on participants’ cognitive performance and depressive symptoms are presented in Table 5.1.

Participants had an average of 5.74±1.28 (3 to 10) of included nights of Zeo data. Descriptive statistics of participants’ average sleep, including comparisons with NSF

\(^{14}\) Analysis was run both with and without these 14 participants and findings for models with REM, SOL, and SWS did not change. One previously significant result in the WASO model became non-significant (identified below).
Chapter 5: Sleep Architecture (Zeo) and Prospective Memory in Older Adults

Table 5.1. Descriptive statistics on cognition and depressive symptoms (N = 103)

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time-based PM (MIST)</td>
<td>5.49 (1.31)</td>
<td>0-8</td>
</tr>
<tr>
<td>Event-based PM (MIST)</td>
<td>6.86 (1.33)</td>
<td>2-8</td>
</tr>
<tr>
<td>Depressive symptoms (PHQ-9 with sleep item)</td>
<td>2.55 (2.98)</td>
<td>0-12</td>
</tr>
<tr>
<td>Depressive symptoms (PHQ-8 without sleep item)</td>
<td>1.92 (2.39)</td>
<td>0-10</td>
</tr>
<tr>
<td>Attention (TEA TS)</td>
<td>3.86 (1.17)</td>
<td>2.25-10.95</td>
</tr>
<tr>
<td>Retrospective Memory (RBANS)</td>
<td>104.42 (11.08)</td>
<td>71-126</td>
</tr>
<tr>
<td>Executive Function factor score</td>
<td>23.85 (7.45)</td>
<td>6.64-42.52</td>
</tr>
</tbody>
</table>

Note. Time-based PM (MIST) = total score on the time-based prospective memory subscale of the Memory for Intentions Screening test, possible scores 0-8, higher scores indicate better performance; Event-based PM (MIST) = total score on the event-based prospective memory subscale of the Memory for Intentions Screening Test, possible scores 0-8, higher scores indicate better performance; PHQ-9 = Patient Health Questionnaire- 9 item version (including sleep item), possible scores 0-27, higher scores indicate more reported depressive symptoms, scores of 5 or above indicate mild depression; PHQ-8 = Patient Health Questionnaire 8-item version (sleep item removed), possible scores range from 0-24, higher scores indicate more reported depressive symptoms; TEA TS = Test of Everyday Attention, telephone search task, higher scores indicate better performance; RBANS = The Repeatable Battery for the Assessment of Neuropsychological Status (delayed memory index) higher scores indicate better performance; Executive function factor score = component score of four executive function measures: Trails B, Digit span backward, COWA Verbal fluency (C and Actions), higher scores indicate better performance.

recommendations based on Hirshkowitz et al. (2015) and Ohayon et al. (2017) are presented in Table 5.2. The correlations for the predictor variables ranged from negligible (< .30) to moderate (.70) based on criteria outlined by Mukaka (2012): REM and SWS (r = -.20, p = .044); REM and SOL (r = .03, p = .732); REM and WASO (r = -.20, p = .038); SWS and WASO (r = -.38 p < .001); SWS and SOL (r = -.22 p = .023); WASO and SOL (r = -.67 p < .001).

Both time-based and event-based PM were regressed on all four sleep variables controlling for covariates (a total of eight models, Table 5.3). Investigation of the covariates showed that older age was significantly associated with poorer scores on time-based PM, B (standard error) = -0.05 (.019), p = .006; and poorer event-based PM, -0.04 (.019), p = .035.

---

15 Inspection of descriptive statistics indicated that n = 11 participants had more than the recommended amount of REM. Analysis run with and without these participants did not change results.
Participant years of education did not significantly predict either time-based PM, B

(standard error) = .01 (.036), p = .776, or event- based PM, - .05 (.037), p = .175.

Table 5.2. 
**Descriptive statistics on variables of EEG defined sleep parameters (N = 103)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
<th>Range</th>
<th>Proportions consistent with NSF recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zeo - SWS (minutes)</td>
<td>44.65 (23.51)</td>
<td>9.09 – 140.72</td>
<td>N/A</td>
</tr>
<tr>
<td>Zeo - SWS (% of TST)</td>
<td>11.62 (5.55)</td>
<td>2.55 – 29.82</td>
<td>100% (n = 103)</td>
</tr>
<tr>
<td>Zeo - REM (minutes)</td>
<td>104.07 (42.37)</td>
<td>16.5 – 236.86</td>
<td>N/A</td>
</tr>
<tr>
<td>Zeo - REM (% of TST)</td>
<td>27.47 (10.69)</td>
<td>5.24 – 64.77</td>
<td>89.32% (n = 92)</td>
</tr>
<tr>
<td>Zeo - Light sleep (minutes)</td>
<td>234.06 (54.88)</td>
<td>19 – 343.42</td>
<td>N/A</td>
</tr>
<tr>
<td>Zeo - Light sleep (% of TST)</td>
<td>60.91 (10.43)</td>
<td>23.22 – 83.38</td>
<td>98.06% (n = 101)</td>
</tr>
<tr>
<td>Zeo - SOL (minutes)</td>
<td>22.89 (17.52)</td>
<td>3 – 80.5</td>
<td>75.73% (n = 78)</td>
</tr>
<tr>
<td>Zeo - WASO (minutes)</td>
<td>55.75 (54.99)</td>
<td>1.84 – 295</td>
<td>41.75% (n = 43)</td>
</tr>
<tr>
<td>Zeo – TST Minutes</td>
<td>382.49 (64.13)</td>
<td>81.835 – 475.5</td>
<td>27.18% (n = 28)</td>
</tr>
<tr>
<td>Zeo – TST Hours</td>
<td>6.37 (1.07)</td>
<td>1.36 – 7.93</td>
<td>65.05% (n = 67)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7.77% (n = 8) short sleepers</td>
</tr>
</tbody>
</table>

**Note.** NSF= National Sleep Foundation; % of TST = average time in each stage as a proportion of total sleep time; SWS = average time per night in slow wave sleep measured with Zeo, NSF consensus recommendations for older adults not reached. REM = average time per night in rapid eye movement sleep measured with Zeo, NSF consensus ≤ 40% of TST unclear, ≥ 41% of TST inappropriate; time in light sleep = average time per night spent in light sleep, NSF consensus ≤ 80% of TST unclear, ≥ 81% of TST inappropriate; SOL = average sleep onset latency per night measured with Zeo, NSF consensus ≤ 30 minutes appropriate, 31-60 minutes unclear, ≥ 61 minutes inappropriate; WASO = average time per night in wake after sleep onset measured with Zeo, NSF recommendation ≤ 30 minutes appropriate, ≥ 31 unclear; TST = average total sleep time measured with Zeo, < 5 hours and > 9 hours scored in inappropriate range; N/A= not applicable as no recommendations are available.

**Direct relationships between PM and EEG defined SWS, REM and SOL and WASO**

Neither the total effect of sleep on time-based PM (Table 5.3, Model 1-4; paths c), nor the direct effect (path c’) were significant. The same was true of event-based PM (Table 4.2, Model 5-8; paths c and c’). That is, no measure of sleep quality significantly predicted performance on either PM subtype.

**Indirect paths between EEG defined SWS, REM and sleep continuity**

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Chapter 5: Sleep Architecture (Zeo) and Prospective Memory in Older Adults

To assess for possible indirect relationships between sleep and PM measures, the a, b and ab paths in each of the eight regression analyses were inspected.

Greater depressive symptoms were predicted by less SWS, more SOL and more WASO (Table 5.3, models 2-4 and 5-8, path a1) but were not predicted by REM (Table 5.4, models 1 and 5, path a1). More SWS also significantly predicted better RM performance (Table 5.4, model 2 and 7, a path 3), but RM was not significantly predicted by any other sleep variable. There were no other significant a paths observed (between sleep variables and attention or EF).

There were no significant b paths observed in any of the models (no significant relationships between depressive symptoms attention, EF, RM and time- and event-based PM; Table 5.3, models 1-8, path b 1-4).

Despite no significant b paths, there were three significant indirect relationships observed, which indicated that less SWS and longer SOL and WASO predicted poorer time-based PM, via greater depressive symptoms (Table 5.3, models 2-4, ab path 1). This was not observed with REM sleep (Table 5.3, model 1, ab path 1). There were no other significant indirect relationships between sleep and either type of PM via depressive symptoms, attention, EF or RM (Table 5.3, models1-4 ab paths 2-4; models 5-8, paths 1-4).

---

16 SWS was no longer significantly predictive of depressive symptoms when calculated as a proportion of TST.
17 The significant indirect relationship between SWS, depressive symptoms and time-based PM became non-significant when SWS was calculated as a proportion of TST.
18 The significant indirect relationship between WASO and time-based PM via depressive symptoms became non-significant when participants with diagnosed sleep disorders (n = 14) were removed from analysis. This change is likely due to a reduction in degrees of freedom.
Table 5.3
Sleep Architecture and Prospective Memory in Older Adults: Possible Pathways

<table>
<thead>
<tr>
<th>Model</th>
<th>Predictor</th>
<th>Mediator</th>
<th>DV</th>
<th>$a$</th>
<th>$b$</th>
<th>$ab$</th>
<th>$c$</th>
<th>$c'$</th>
<th>Covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Time in REM</td>
<td>Depressive Symptoms</td>
<td>Time-based PM</td>
<td>B = -0.003</td>
<td>B = -0.12</td>
<td>B = 0.0003 (−0.0001 to 0.001)</td>
<td>B = 0.001</td>
<td>B = 0.001</td>
<td>Age, years of education.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Attention</td>
<td></td>
<td>B = 0.001</td>
<td>B = -0.11</td>
<td>B = 0.0001 (−0.0003 to 0.001)</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Executive Function</td>
<td></td>
<td>B = 0.004</td>
<td>B = 0.03</td>
<td>B = 0.0001 (−0.0003 to 0.001)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Retrospective Memory</td>
<td></td>
<td>B = -0.01</td>
<td>B = 0.004</td>
<td>B = -0.00004 (−0.001 to 0.0003)</td>
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</tr>
<tr>
<td>2</td>
<td>Time in SWS</td>
<td>Depressive Symptoms</td>
<td>Time-based PM</td>
<td>B = -0.01†</td>
<td>B = -0.11</td>
<td>B = 0.001* (0.0001 to 0.004)</td>
<td>B = -0.0001</td>
<td>B = -0.003</td>
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</tr>
<tr>
<td>Event</td>
<td>Depressive Symptoms</td>
<td>Time-based PM</td>
<td>B</td>
<td>B</td>
<td>B</td>
<td>B</td>
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<tr>
<td><strong>Attention</strong></td>
<td></td>
<td></td>
<td>B = 0.004</td>
<td>B = -0.13</td>
<td>B = 0.001</td>
<td>(-0.0003 to 0.003)</td>
<td>Age, years of education.</td>
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<tr>
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<td>B = 0.02</td>
<td>B = 0.0004</td>
<td>(-0.0002 to 0.002)</td>
<td>Age, years of education.</td>
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<tr>
<td><strong>Retrospective Memory</strong></td>
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<td></td>
<td>B = 0.05†</td>
<td>B = 0.01</td>
<td>B = 0.0003</td>
<td>(-0.001 to 0.003)</td>
<td>Age, years of education.</td>
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<tr>
<td><strong>Sleep Onset Latency</strong></td>
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<td>Time-based PM</td>
<td>B = 0.02†</td>
<td>B = -0.11</td>
<td>B = -0.002*</td>
<td>(-0.01 to -0.0003)</td>
<td>Age, years of education.</td>
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<tr>
<td><strong>Attention</strong></td>
<td></td>
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<td>B = 0.01</td>
<td>B = -0.12</td>
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<td>(-0.003 to 0.0004)</td>
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<td>B = 0.03</td>
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<td>(-0.003 to 0.0001)</td>
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<td></td>
<td>B = -0.06</td>
<td>B = 0.004</td>
<td>B = -0.0003</td>
<td>(-0.003 to 0.001)</td>
<td>Age, years of education.</td>
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<tr>
<td><strong>Wake After Sleep Onset</strong></td>
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<td>Time-based PM</td>
<td>B = 0.01‡</td>
<td>B = -0.12</td>
<td>B = -0.001*</td>
<td>(-0.002 to -0.0001)</td>
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<td>(-0.001 to 0.0001)</td>
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<td>B = -0.01</td>
<td>B = 0.02</td>
<td>B = -0.0002</td>
<td>(-0.001 to 0.0004)</td>
<td>Age, years of education.</td>
<td></td>
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<tr>
<td><strong>Retrospective Memory</strong></td>
<td></td>
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<td>B = -0.01</td>
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<td>(-0.001 to 0.0003)</td>
<td>Age, years of education.</td>
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<tr>
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<td>Depressive Symptoms</td>
<td>Event-based PM</td>
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<td>B = -0.01</td>
<td>B = 0.00003</td>
<td>(-0.0003 to 0.001)</td>
<td>Age, years of education.</td>
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<td>B = -0.003</td>
<td>B = -0.00000</td>
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<td>Age, years of education.</td>
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<td>B = -0.04</td>
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<td>Age, years of education.</td>
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<tr>
<td>Event</td>
<td>Depressive Symptoms</td>
<td>Attention</td>
<td>Executive Function</td>
<td>Retrospective Memory</td>
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<tr>
<td><strong>6 Time in SWS</strong></td>
<td>B = -0.01</td>
<td>B = 0.02</td>
<td>B = -0.01†</td>
<td>B = 0.05†</td>
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<td><strong>Depressive Symptoms</strong></td>
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<td>B = -0.03</td>
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<tr>
<td><strong>Age, years of education</strong></td>
<td>B = 0.0004</td>
<td>B = 0.002</td>
<td>B = 0.0001</td>
<td>B = 0.0001</td>
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<tr>
<td><strong>Time in SWS</strong></td>
<td>0.001 to 0.002</td>
<td>0.001 to 0.002</td>
<td>0.001 to 0.002</td>
<td>0.001 to 0.002</td>
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<tr>
<td><strong>Attention</strong></td>
<td>0.001 to 0.002</td>
<td>0.001 to 0.002</td>
<td>0.001 to 0.002</td>
<td>0.001 to 0.002</td>
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<td><strong>Executive Function</strong></td>
<td>0.001 to 0.002</td>
<td>0.001 to 0.002</td>
<td>0.001 to 0.002</td>
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<tr>
<td><strong>Retrospective Memory</strong></td>
<td>0.001 to 0.002</td>
<td>0.001 to 0.002</td>
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<td>0.001 to 0.002</td>
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<td><strong>Age, years of education</strong></td>
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<td>0.001 to 0.002</td>
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<tr>
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<td>B = 0.04</td>
<td>B = 0.004</td>
<td>B = 0.001</td>
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<tr>
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<td>B = 0.04</td>
<td>B = 0.004</td>
<td>B = 0.001</td>
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<tr>
<td><strong>Age, years of education</strong></td>
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<td>B = 0.006</td>
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<tr>
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<td>-0.002 to 0.001</td>
<td>-0.001 to 0.002</td>
<td>-0.01 to 0.0003</td>
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<tr>
<td><strong>Executive Function</strong></td>
<td>-0.002 to 0.001</td>
<td>-0.001 to 0.002</td>
<td>-0.01 to 0.0003</td>
<td>-0.01 to 0.0003</td>
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<tr>
<td><strong>Retrospective Memory</strong></td>
<td>-0.001 to 0.002</td>
<td>-0.001 to 0.002</td>
<td>-0.01 to 0.0003</td>
<td>-0.01 to 0.0003</td>
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<tr>
<td><strong>Age, years of education</strong></td>
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<td>0.001 to 0.002</td>
<td>0.001 to 0.002</td>
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<tr>
<td><strong>Wake after sleep onset</strong></td>
<td>B = 0.01‡</td>
<td>B = -0.03</td>
<td>B = 0.0002</td>
<td>B = 0.001</td>
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<td>B = 0.04</td>
<td>B = 0.0002</td>
<td>B = 0.001</td>
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<td><strong>Event-based PM</strong></td>
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<td>B = -0.02</td>
<td>B = 0.0004</td>
<td>B = 0.001</td>
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</tr>
<tr>
<td><strong>Age, years of education</strong></td>
<td>B = 0.0004</td>
<td>B = 0.0004</td>
<td>B = 0.00003</td>
<td>B = 0.0001</td>
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<tr>
<td><strong>Attention</strong></td>
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<td>-0.001 to 0.0003</td>
<td>-0.0003 to 0.001</td>
<td>-0.0001</td>
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<td><strong>Executive Function</strong></td>
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<td>-0.0003 to 0.001</td>
<td>-0.0001</td>
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<td>-0.001 to 0.0002</td>
<td>-0.001 to 0.0002</td>
<td>-0.0001</td>
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</table>

*Note. N = 103; REM = average number of minutes in rapid eye movement sleep across all nights measured with Zeo; SWS = average time spent in slow wave sleep across all nights measured with Zeo; Sleep onset latency = time taken to fall asleep averaged across all nights measured with Zeo, WASO = average number of minutes spent in wake after sleep onset across all nights measured with Zeo, Time-based PM (MIST) = total score on the time-based prospective memory subscale of the Memory for Intentions Screening Test, higher scores indicate better performance; Event-based PM (MIST) = total score on the event-based prospective memory subscale of the Memory for Intentions Screening Test, higher scores indicate better performance; depressive symptoms = total score on Patient Health Questionnaire 8-item version (sleep item removed), higher scores indicate more reported depressive symptoms; Attention = score on the Test of Everyday Attention, telephone search task, higher scores indicate better performance; Retrospective Memory = The Repeatable Battery for the Assessment of Neuropsychological Status, delayed memory index score, higher scores indicate better performance; executive function = component score of four executive function measures: Trails B, Digit span*
backward, COWA Verbal fluency (C and Actions), higher scores indicate better performance. DV = dependent variable; † = significant at p < .05, ‡ = significant at p < .001; B = effect size; a = path between the predictor and the mediator; b = path between the mediator and outcome variable; ab = indirect path (via the mediator) between the predictor and outcome variable, presented as effect size, B (bootstrapped 95% confidence interval [CI]); c = total effect of the predictor on the outcome variable; c’ = direct effect of the predictor on outcome variable, independent of the pathway through the mediator; * = significant effect as CIs do not cross zero. Where confidence intervals are exactly 0.00, up to 5 decimal places are presented.
Chapter 5: Sleep Architecture (Zeo) and Prospective Memory in Older Adults

**Discussion**

This study aimed to investigate the possible relationships between habitual EEG-defined sleep architecture and PM in community-dwelling older adults. Contrary to our first hypothesis, there were no overall relationships observed between any of the sleep and PM measures. This result, while contrary to expectations, is consistent with the findings of the previous two studies in this thesis, which also did not observe direct relationships. It had been hypothesised that using EEG to assess sleep (rather than activity monitoring or self-report) could reveal direct relationships not found in previous studies. However, instead, these findings have again suggested that sleep and PM may not be related in older adults, except via depression, regardless of PM subtype (event- or time-based).

This first hypothesis was based largely on previous research suggesting that sleep architecture is important for multiple areas of cognitive functioning, and therefore is likely to also be important for PM (Blackwell, Yaffe, Ancoli-Israel, et al., 2011; Della Monica et al., 2018; Groeger et al., 2014; Scullin & Bliwise, 2015a, 2015b; Song et al., 2015; Walker, 2009). Findings in the present study did not suggest that sleep consistently predicted any of these variables either, although this varied across sleep parameters. SWS did not predict attention or EF, contrary to Della Monica et al. (2018) and Scullin et al. (2015). However results did show that less time in SWS predicted greater depressive symptoms as well as poorer RM, largely consistent with expectations based on available research (Della Monica et al., 2018; Edinger et al., 2000; Groeger et al., 2014; Scullin & Bliwise, 2015a; Walker, 2009). It was, therefore, surprising that this did not extend to PM performance, as both of these functions are important for PM.
Also surprising was that the total time spent in REM did not predict any of the cognitive variables or reported depressive symptoms. This is not consistent with studies that have shown that PSG-defined time in REM can predict global cognition (e.g. on MMSE scores) as well as poorer executive functioning, processing speed and episodic retrospective memory, both cross-sectional and longitudinally (Blackwell, Yaffe, Ancoli-Israel, et al., 2011; Della Monica et al., 2018; Song et al., 2015).

Of note, the current study design considers REM and SWS as absolute values (i.e. total number of minutes) rather than proportions of TST, as is done in some other research. Given that analyses in the current study were run both ways (total minutes, as well as proportionate to TST), and still did not produce direct results, it does not appear that this variation in methodology explains these null findings.

The absence of overall effects was not exclusive to sleep architecture; there were also no significant relationships between EEG-defined sleep continuity (SOL or WASO) and cognition, which was unexpected. This is contrary to previous research (Brewster et al., 2015; Waters & Bucks, 2011) but is consistent with results in the previous study which calculated these measures calculated with actigraphy. Again, as with the previous study, it may be that there are other factors specific to our sample that have influenced these results.

This sample appears to have sufficient variability in both the predictor (PM) variables. Although the majority of participants scored well on the PM scales, there was a wide range of scores with some participants scoring close to the minimum possible.

Likewise, there appears to be sufficient variability in the sleep measures. While it is difficult to conclude if our participants had appropriate amounts of each of REM or SWS, given that recommendations are largely unclear (Ohayon et al., 2017) there was a wide
range of time spent in each stage in this sample. Of note, this sample had more variability of SOL in comparison to the previous study. Almost a quarter of participants had SOL longer than the recommended 30 minutes, whereas in the previous study, SOL measured with actigraphy showed 100% falling into this range. This supports previous research that has questioned the reliability of actigraphically-defined SOL (J. L. Martin & Hakim, 2011). With regards to WASO, just over one third of participants had WASO classified as appropriate (Ohayon et al., 2017). However, as discussed in the previous chapter this estimate may be too restrictive for older adults. Again, lack of NSF consensus made it difficult to interpret how many participants had problematic WASO, but there was variability in the range. While the variability in the sleep measures may be explained, in part, because participants with diagnosed sleep disorders were kept in the sample, analyses run with and without these participants did not significantly change this non-significant result, and so this does not appear to be a driver for the observed findings for this hypothesis. Conversely, perhaps if we had more participants with sleep disorders/poor sleep for other reasons, the increase in variability may have resulted in a significant effect.

The second hypothesis in this study was that there are indirect relationships between sleep and PM. Consistent with this, results did demonstrate multiple significant indirect relationships between sleep and PM via depressive symptoms. The novel finding in this study is that more time spent in SWS, but not REM, predicted greater self-reported depressive symptoms, which in turn predicted poorer time-based, but not event-based PM performance. The previous two studies suggested that this same relationship exists based on TST, not specifying which type of sleep. Therefore, the current results build on these
previous finding suggesting that it is additional time in SWS in particular that may be driving the impact of total sleep time on time-based PM via depression.

Consistent with the previous study that looked at sleep continuity, these findings again demonstrated that more WASO also predicted poorer time-based PM via depressive symptoms. However, contrary to Study 2, this study also found this same indirect relationship with SOL as the predictor. Finding this indirect relationship with EEG-measured SOL, but not actigraphically-measured SOL (as in Study 2) again supports the claim that actigraphy may be limited in it’s ability to assess this measure (J. L. Martin & Hakim, 2011). Conversely, the Zeo had the ability to code sleep based on EEG signals and so may have detected sleep onset more reliably.

Broadly speaking, these results appear to echo the findings of the previous studies in this thesis, again suggesting that an indirect relationship appears to exist between sleep and PM via depressive symptoms. This is consistent with previous research that has repeatedly demonstrated depressive symptoms as being related both to poorer sleep quality and to PM performance (Riemann, Berger, & Voderholzer, 2001; Tsuno, Besset, & Ritchie, 2005). Importantly, these findings were only for time-based but not event-based PM, which, consistent with MPT, suggests that the more cognitively demanding PM sub-type may have been more sensitive to the effects of mild sleep and depressive symptoms.

Surprisingly, there were no significant indirect relationships via any of the cognitive variables. This is perhaps explained in part by the inconsistent predictability of sleep on the various areas of cognitive functioning. However, even when sleep did predict other cognitive functions (e.g. SWS predicted RM), this did not in turn predict PM performance. In fact, these results suggested that none of the cognitive variables significantly predicted
either type of PM in this sample. This is surprising, as previous research suggests that attention, RM and EF are all important for PM (McDaniel & Einstein, 2007). In the case of attention and EF, this may be because of a lack of variability in performance, given that these variables did not have a significant association with any of the predictor (sleep) or outcome (PM) measures. However, in the case of RM, this is less clear: descriptive statistics indicate a wide range of scores and the significant relationship with SWS suggests sufficient variability. It seems likely then, that, as with the first hypothesis, these null findings may have been influenced by the limited variability in the PM measures, which were not sensitive enough to individual differences in RM.

Results may also have varied in comparison to previous findings because of differences in design and methodology. The majority of previous studies using measures of sleep architecture do so with PSG, which is considered to be the gold standard for sleep assessment (Michaelson, Allan, Chaney, & Mair, 2006). While the Zeo has been found to be a sufficient substitute for PSG and has several notable advantages, it is less accurate in detecting sleep architecture than PSG (Shambroom et al., 2012). Moreover, many studies which have looked at sleep and cognition rely on only one night of PSG data (Blackwell, Yaffe, Ancoli-Israel, et al., 2011; Della Monica et al., 2018; Song et al., 2015), and other studies have systematically manipulated sleep e.g. SWS restriction (Ferrara et al., 2000; Groeger et al., 2014). Even in studies that do not manipulate sleep, it is likely that a PSG study with no adjustment period will result in some acute sleep disruption (i.e. first night effect), due the change in environment and intrusive equipment (Blackwell et al., 2017). In contrast, the current study assessed habitual sleep quality using non-intrusive sleep equipment which participants used in their own bed for multiple nights. This likely meant
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that the sampled sleep was more representative of typical patterns, rather than reflecting an acute sleep interruption. We know that, in the long term, habitual poor sleep can have marked consequences, including increased risk of dementia (Spira, Chen-Edinboro, Wu, & Yaffe, 2014), however, in the short term, poor habitual sleep may have more subtle effects on cognition than acute deprivation: where sleep is consistently and chronically affected, the person may have a chance to compensate or adjust to their sleeping patterns. It is difficult to read too much into this, as our measurement was just for one week, and we do not know how long our participants’ sleep had been at this quality, or if the weeks’ sleep assessed was representative of their typical sleeping pattern. On the other hand, one night of bad sleep may be counteracted in the context of a week of otherwise good sleep, and may not have the same significant outcomes as occurs with acute sleep loss. Of note, at least one other study has assessed multiple nights of sleep, finding results comparable to the present study (i.e. more deep sleep predicted better attentional performance; Edinger et al., 2000). However, there are insufficient studies of this nature to draw broader conclusions.

There are also some sample characteristics in this study that differ to samples used in previous research. For example, while Scullin et al (2015) found a relationship between RM and time spent in REM, they used a clinical sample of participants with Parkinson’s disease. Ferrara et al. (2000) observed that poorer sleep was associated with slower processing speed, but this was in a younger sample (20-30 years). As our sample were non-clinical older adults, these findings are not directly comparable, and these sample differences may partly explain the differences in findings.

As in the previous two studies, education did not significantly predict either sub-type of PM in these analyses, however it is possible that the overall high education in this sample
protected against the effects of sleep loss (cognitive reserve) which is discussed in Chapter 6 (Farfel et al., 2013).

This study has several notable strengths which make it a valuable contribution to the literature. The study design recruited a relatively large sample, and used a comprehensive cognitive assessment which gave us valid measures of several cognitive domains including PM. This study also utilised a non-intrusive method of EEG sleep measurement which, although not as comprehensive as overnight PSG, assesses more naturalistic sleep quality in the participants’ own homes. This form of assessment has previously not been available, however as technology in this area continues to grow, research of this nature may also grow accordingly in the future (Hamida et al., 2015).

It is important to note that because these results are cross-sectional, directions of these results cannot be inferred. It could be that depressive symptoms are predicting both sleep and PM, and there is no causal relationship between the two variables. To build on these findings, future studies could look at the relationship between sleep architecture using longitudinal data, which would allow for inferences regarding causality. Building on this research, there are several possible avenues to explore additional research, and these are discussed in the general discussion of this thesis.

Overall, the findings of this study do not suggest that an overall relationship exists between sleep architecture and PM performance in older adults. However, they do, again, suggest indirect relationships between sleep (SWS, SOL and WASO) with time-based PM, via self-reported depressive symptoms.
Chapter 6: General Discussion
CHAPTER 6

General Discussion

Overview of Aims and Hypotheses

The overarching aims of this thesis were to investigate the relationship between sleep and prospective memory (PM) in community-dwelling older adults. This thesis also investigated the potential roles of other variables known to be important for sleep, PM and ageing, i.e. depressive symptoms, attention, executive function (EF) and retrospective memory (RM). Given the multitude of ways that sleep quality can be considered, each of the three studies in this thesis took a different approach to sleep assessment using validated measures of 1) subjective sleep; 2) objective sleep continuity and duration and; 3) objective sleep architecture and continuity. Using these varied approaches to sleep measurement, as well as validated measures of depressive symptoms and cognition, two specific hypotheses were proposed:

1. That there is a relationship between sleep and PM, specifically:
   a. That better sleep quality would predict better PM performance.
   b. That the relationship would be stronger in more cognitively demanding PM tasks (i.e. time-based vs. event-based).

2. That the relationship between sleep and PM might be mediated by, or operate via:
   a. Self-reported depressive symptoms
   b. Attention
   c. Retrospective memory (RM)
   d. Executive function (EF)

Brief Overview of Findings:
General Discussion

The first study of this thesis investigated whether self-reported sleep would predict PM abilities in a sample of 170 community dwelling older adults (50-93 years). Sleep was measured using the Pittsburgh Sleep Quality Index component scores of sleep onset latency (SOL), sleep efficiency, sleep disturbance and sleep duration. PM was assessed using the memory for intentions screening test (MIST), both time-based and event-based subscales. Participants were also assessed for self-reported depressive symptoms, and were tested for performance on measures of EF, RM and attention. Total numbers of years of education as well as age (years) were entered as covariates, as they both are related to sleep and cognition. Results did not support the presence of an overall relationship between sleep and PM, which was surprising in the context of extant theory and research. However, indirect relationships between sleep and PM via symptoms of depression were observed, with poorer sleep predicting an increase in reported depressive symptoms, which in turn predicted poorer PM. This was true for all self-reported sleep variables and PM performance, regardless of level of cue type.

Study 2 was similar in design and aims to Study 1, and investigated the relationship between sleep and PM, but using objectively measured sleep continuity. Specifically, actigraphy was used to provide estimates of sleep duration, SOL and wake after sleep onset (WASO). The study used the same measures of depressive symptoms and cognition (including PM) as in Study 1, and the same covariates. Participants were 133 community-dwelling older adults (age 50-93), with 49 participants in this sample also included in Study 1. The primary difference was that we hypothesised indirect rather than mediated effects, given Study 1 results. Findings were similar to Study 1, showing no overall relationships between sleep and PM. Although this was consistent with Study 1, it was still a surprising
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result because we had anticipated that using an objective measure would yield significant effects. However, several indirect effects were observed between sleep and time-based PM, again via depressive symptoms. This was true for TST and WASO, but not SOL, and was not observed with event-based PM.

Finally, Study 3 again had similar design and aims, this time using estimates of sleep architecture collected obtained from a portable, single electrode EEG device (ZEO) over multiple nights. The primary sleep parameters of interest were Rapid Eye Movement (REM) sleep and Slow Wave Sleep (SWS), and the study also looked at SOL and WASO but calculated with EEG rather than movement as in the previous study. Measures of cognition and depressive symptoms, as well as covariates, were the same as in the previous studies in this thesis. As with Study 2, we hypothesised indirect effects via depression, RM, attention and EF, rather than mediated effects. Participants were 104 community dwelling older adults (age 50-90), with 58 participants in this sample also included in Study 2, but no overlap with the cases in Study 1. Again, results did not suggest any overall relationships between sleep and PM, although indirect relationships were observed between sleep (all measures apart from REM) and time-based PM via depressive symptoms.

Discussion of Findings

**Hypothesis 1 – overall relationships between sleep and PM.**

The central aim of this thesis was the investigation of the potential, overall relationship between sleep and PM. None of our findings supported this hypothesis. Given that we investigated this with a range of approaches to sleep measurement, it seems unlikely that this null finding could be attributed to how sleep was measured. In each of the studies we considered if these null findings may have been influenced by the variability of the
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measures used, specifically the high performance in PM, by the covariates (age and years of education), or by specific characteristics of our samples that differed to the previous research that informed our hypotheses. In Study 3, we also considered the different ways that REM and SWS are measured (raw minutes vs. % of TST).

These null findings meant that we could not investigate the second part of this hypothesis as planned (that more demanding PM tasks would be more strongly associated with poor sleep). However, there were differences seen between time-based and event-based performance in terms of the significant indirect effects, which are discussed below.

**Hypothesis 2 – mediations (Study 1)/indirect relationships (Studies 2 and 3).**

It was originally hypothesised that the relationship between sleep and PM would be fully or partially mediated by either depressive symptoms, EF and RM or attention. However, given that there were no significant relationships found between these variables, mediation could not be explored. When this became apparent in the first analysis, we investigated the potential presence of indirect effects, which, argued by Hayes (2013) may be present even in the absence of direct or total effects. Results suggested that sleep was indirectly associated with PM. After this pattern was observed in the first study, the second two studies did not hypothesise mediations, instead focussing on possible indirect relationships. The findings of these studies are discussed in turn as follows:

2 a) **Depressive symptoms.**

Arguably the most important and consistent finding across all three studies was the presence of a significant indirect relationship between sleep and PM via depressive symptoms. That is, poorer sleep quality predicted greater depressive symptoms which, in turn, predicted poorer PM. In the first study, this was true for all of the four sleep variables
investigated, with both time-based and event-based PM. In Study 2, this was true for WASO and sleep duration with time-based but not event-based PM. For Study 3, this was true for SOL, WASO and SWS, again, only in the time-based subtype. To summarise, this indirect relationship was found between time-based PM and all measures of sleep apart from SOL measured with actigraphy and time in REM measured with the Zeo.

Considered together, these results strongly suggest that depressive symptoms play a key role in the relationship between sleep and PM in older adults. This was consistently true for time-based PM but not event-based PM, with only Study 1 yielding significant indirect effects for the latter. It is possible that this inconsistency owes to the larger sample size in the first study, which may have increased sensitivity of findings. Alternatively, it may be that those participants who reported increased depressive symptoms may have had a negative bias in their self-reported sleep complaints, potentially inflating the relationship between sleep quality and depressive symptoms. If this were true, this inflation would be controlled for in the subsequent studies, which had the advantage of objective sleep measurement.

Importantly, given that the majority of participants did not meet criteria for clinical depression, it seems that even sub-clinical depressive symptoms may have important implications for cognition. This is consistent with ample previous research that has suggested self-reported depressive symptoms predict cognitive abilities, including PM (Y. R. Li et al., 2014; Y. R. Li et al., 2013). It is also consistent with previous research that points to sleep as being important for depressive symptoms (Riemann et al., 2001). Although, these cross-sectional findings cannot confirm causation, they do suggest that
depressive symptoms play a linking role between sleep and PM, which to the authors’ knowledge has not been reported previously.

It was interesting that the indirect relationship between SOL and PM via depressive symptoms was significant in Studies 1 and 3 but not Study 2. As discussed in Chapters 4 and 5, there are some inherent limitations in assessing SOL using actigraphy which may explain this discrepancy in results (Martin, 2011). Specifically, as actigraphy is based on physical movement, it may have overestimated how quickly sleep began, possibly because participants were lying still when they were trying to fall asleep: a fact of which they would have been aware. This is consistent with the descriptive statistics, in Study 2, which show that on average participants took fewer than 5 minutes to fall asleep, and 100% of participant were within the NSF recommended range of SOL (Ohayon et al., 2017).

It was also surprising that an indirect relationship was not observed with time spent in REM. As discussed in Chapter 5, this may reflect a non-linear relationship between REM, sleep and depressive symptoms. While REM sleep is restorative and important for cognitive and psychological health, too much REM sleep may be detrimental to depressive symptoms and cognition (McGrath & Cohen, 1978; Vogel, Vogel, McAbee, & Thurmond, 1980). Given that some participants in our Study 3 sample had an above optimal level of REM (i.e. above 40% of TST), it is possible that this is why no significant relationships were observed (Ohayon et al., 2017). It is not clear from the available data why some participants exhibited these high percentages of REM sleep.

Of note, in Study 1, the indirect relationship via depressive symptoms was observed in both time-based and event-based PM, whereas with Studies 2 and 3, this indirect path was only observed in time-based PM. Interestingly, this appears to support the second part of
the first hypothesis, that time-based sleep is more likely to be affected. However, it is unclear why subjective sleep did not also show this pattern.

2b) **Attention.**

The findings of this thesis did not support the hypothesis that sleep and PM were related via attention (no significant indirect paths were observed). As outlined in the general introduction of this thesis, the state instability hypothesis is that decreased arousal and vigilance predict cognitive deficits following sleep loss (Doran et al., 2001). In contrast to this, no sleep variables predicted attention in the present research. Importantly however, the conclusions drawn by Doran et al. (2001) are based on total acute sleep deprivation, which results in notable interruptions to vigilance because of fatigue. It may be that the more subtle variations in our participants’ habitual sleep quality were not sufficiently severe to produce attention deficits. Perhaps a more drastic interruption to sleep, i.e. in a sleep deprivation study, may have been more likely to show the relationship between sleep and attention. Moreover, these null results may reflect limitations of the attention measure used: while the TEA is a well-established measure which correlates with other measures of attention (Robertson, 1996), it is possible that the single sub-test used was not sufficiently sensitive or specific enough to capture individual differences in this cohort. Other measures of attention may have yielded differing results.

However, it is also important to note that attention did not predict PM performance in any of the studies, which is contrary to expectations that attention is needed to monitor the environment for the cue that a task needs to be completed.

2c) **Executive function (EF)**
General Discussion

The final hypothesis outlined in the general introduction was that sleep may impact cognition via a direct influence on parts of the brain that then influence cognition (i.e. the frontal and temporal lobes; Beebe & Gozal, 2002). This theory led us to predict that PM may be predicted by EF deficits caused by poor sleep, given that EF is linked to frontal lobe function and is important for successful PM. Conversely to this theory, however, EF performance was not significantly predicted by any of the sleep measures, subjective or objective, used in this thesis. Although previous literature pertaining to the relationship between EF sleep has been mixed, it would have been expected that at least some of the sleep parameters would have predicted EF, and so these results are surprising (Holanda Júnior & Almondes, 2016). Importantly a notable strength of our study design was that we used a composite factor which incorporated performance on tests which assessed both verbal and visual EF abilities across multiple EF sub-domains including shifting, updating and generativity (Fisk & Sharp, 2004). However, Fisk and Sharp (2004) also identified age-related impairment in inhibition, which was not investigated in the present research. Given that some of the studies that have linked sleep with EF performance have used measures of inhibition (e.g. Gamaldo et al., 2008; Saint Martin et al., 2012) this may have been a limitation of our research design.

2 d) Retrospective Memory (RM).

Continuing on from the above, the hypothesis that sleep affects the brain, also led us to expect that sleep may affect PM via RM, which is linked to the temporal lobes and is important for PM. A single significant indirect effect was observed in Study 1, which suggested that more self-reported total sleep time predicted better time-based PM performance via better RM performance. While this is an interesting finding,
comprehensive subsequent investigation in this thesis failed to replicate this result, suggesting that it may have been an unreliable effect. Of note, RM was associated with self-reported sleep duration (Study 1) as well as time in SWS (Study 3), but not other variables of sleep. These findings largely support previous research suggesting that a relationship between sleep and RM exists, although it is unclear why the relationship was not observed with our actigraphic measures of sleep quality (Waters & Bucks, 2011). Moreover, while RM predicted time-based PM in Studies 1 and 2, it did not predict any other measures of PM, findings that are contrary to the expectations that RM and PM would be closely linked. A strength of the present study is that we assessed RM using an index score of several different RM tests, including both verbal and visual measures. Therefore, it is likely that our approach was sufficiently comprehensive to be compared with previous research investigating RM abilities. However, of note, the current research only considered delayed memory, whereas some of the previous literature found effects in immediate recall (e.g. Scullin et al., 2015).

Covariates.

*Years of education and the possible role of cognitive reserve.* Each of the studies in this thesis co-varied for the total number of years of education. This was done to account for the fact that this variable was likely to correlate with PM abilities. However, surprisingly, years of education and PM were not significantly related in any of the three studies. This is unlikely to be because of lack of variability (while participants generally had high levels of education, there was variability in this measure), or because of exclusion criteria (not significantly different between included vs excluded participants). It may be that the relationship between sleep and PM changes depending on education level, which cannot be
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tested when education is entered as a covariate. An alternative way of approaching this would have been to include this variable as a moderator. Although this was not undertaken in the current studies, it is a method that perhaps should be considered in future research in this field.

Looking at the sample as a whole, our participants are on average quite highly educated (almost 14 years of formal education). This is important, because these education levels may have helped them compensate for sleep related cognitive difficulties (including PM), i.e. served as a means of cognitive reserve (Whalley, Deary, Appleton, & Starr, 2004). There is growing literature that cognitive reserve can serve as a ‘buffer’ against factors that can affect cognition, including ageing and poor sleep (Alchanatis et al., 2005; Zimmerman, Bigal, Katz, Brickman, & Lipton, 2012).

While education is a major active component of cognitive reserve, there are also other important components e.g. IQ, occupational achievement, and increased physical and social activity (Scarmeas & Stern, 2003; Whalley et al., 2004). The HARP sample is primarily comprised of highly-educated, high-functioning and active older adults, often recruited from community interest groups. Considering this, together with the high education, we may infer that our participants have a high level of cognitive reserve, although this was not directly measured. Future studies could try to measure this more directly e.g. assess premorbid abilities with the National Adult Reading Test (NART; Nelson & Willison, 1991) or the Test of Premorbid Functioning (TOPF; Pearson, 2009).

In the absence of the availability of these measures in the current study, we inspected total RBANS scores, to further investigate the representativeness of our sample. Although not a measure of cognitive reserve, these total scores indicate the general cognitive abilities
of our participants, and were normed against similar aged community-dwelling adults. The average RBANS score of all the included participants presented in this thesis was $M = 103.22$, $SD = 13.13$. Although this is slightly higher than those excluded (Chapter 1, Table 1.1), the mean score does not suggest that our participants’ general cognitive functioning was significantly above the average of the normative sample in this age range ($Cohen's \, d = 0.23$)\(^{19}\). Moreover, this finding was similar across the individual studies (Study 1 = 102.99; Study 2 = 103.22; Study 3 = 104.84). Therefore, it seems unlikely that the general cognitive abilities of the sample reported were significantly above other adults of a similar age.

Alternatively, it may be that participants in this research were particularly motivated to do well as they valued the research project and were invested in its success (aside from a small honorarium, there was no other material incentive for participation). This may be especially true for those participants who have invested in the project longitudinally. This is important, because motivated participants may allocate more cognitive resources to the task and perform better than they would have without motivation (Revelle, 1993). Indeed, motivation may play a particularly important role in cognitive performance in older adults: Hess (2014) argues that older adults may be less motivated to engage in cognitively demanding tasks due to increases in the costs of cognitive engagement, and emphasises the importance of considering motivational factors in understanding aging effects on cognitive functioning. Therefore, it could be that the motivation of our participants may have improved performance and even compensated for sleep related-deficits that we may have observed in a less motivated sample.

**Interaction of Age, Sleep and Cognition**

\(^{19}\) The RBANS Total Score has an average of 100 and a standard deviation of 15.
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All analyses in this study also controlled for the effects of age. Results showed that in each of the studies age was significantly predictive of time-based but not event-based PM. However, as with education levels, it may be that rather than directly affecting PM, advancing age influences the relationship between sleep and cognition. To test this, again, age would need to be considered as a moderator, and this could be considered in future studies.

Importantly, these studies looked at sleep and PM only in older adults aged 50+ years, therefore, the broader effects of age on sleep and on PM (i.e. younger vs older adults) would not have been as evident. Future research that is specifically interested in the effect of the ageing process on PM could consider comparing samples of different ages.

All testing for PM in these studies was conducted in controlled, laboratory conditions. However, as noted in the General Introduction, real-world PM abilities may be affected by age differently, marking an age-PM paradox (Schnitzspahn, Ihle, Henry, Rendell, & Kliegel, 2011). This could be an interesting potential avenue for future research, i.e. are there different relationships between sleep and PM in ageing in the context of real-world PM? This would be important, as it is the real-world PM success or failure that is likely to be most important for daily living e.g. turning off the stove or remembering relatives’ birthdays. One way to assess this would be with a naturalistic task that could be completed outside of the laboratory (e.g. asking the participant to phone and wish the researcher a happy birthday), or a self-report diary to inform on daily completed PM tasks.

Alternatively, this could be investigated is with the prospective and retrospective memory questionnaire (PRMQ), a subjective questionnaire, which asks questions about real life memory requirements, including PM, e.g. “Do you decide to do something in a few
minutes’ time and then forget to do it?” (Crawford, Smith, Maylor, Della Sala, & Logie, 2003). To guard against self-report bias (or lack of insight), there is also a proxy version in which a partner or relative can report on memory functioning on the participants’ behalf (Crawford, Henry, Ward, & Blake, 2006). Future studies could investigate sleep, depressive symptoms and cognition, as done in the present research, but using the PM subscale of this measure rather than the MIST. It would be interesting to see if the same indirect effect (via depressive symptoms) would still be observable. Of note however, is that while this approach would offer interesting information about self-reported real-world PM abilities, research with this measure may be less valid in terms of representing true PM abilities. A 2011 study (Uttl & Kibreab), found that self-reported PM performance may be influenced by a range of things, including verbal intelligence, personality, busyness and the use of memory aids/reminders. Therefore, research considering self-report PM would ideally presented as well as, not instead of, objectively measured PM.

**Risk of Type 1 Error due to Multiple Comparisons**

Each of the studies in this thesis used multiple (six-eight) multivariate linear regression models to investigate relationships between two measures of PM (time-based and event-based) and various measures of sleep. It could be argued that adjustments should have been made for multiple comparisons in these analyses (e.g. Weisstein, 2004). However, while correcting for multiple comparisons would have reduced the likelihood of incorrectly rejecting the null hypothesis (type 1 error), it also would have increased the likelihood of missing significant results (type 2 error; Rothman, 1990). Had we adjusted for multiple comparisons (e.g with the Bonferroni method of correction; Weisstein, 2004), some of the results presented in this thesis may not have remained significant. This is especially likely to be true for the indirect relationships between sleep and PM via depression, some of
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which had confidence intervals that came close to crossing zero. Importantly, all hypotheses in this thesis, including their directions, were predicted a-priori based on previous research and theoretical accounts of sleep and cognition\(^{20}\). Therefore, in order to reduce the chances of a type 2 error, we decided not to adjust for multiple comparisons.

Considering the findings of each of the studies together supports this decision. While it is possible that findings in one study may have occurred as a type 1 error, it is unlikely that the same results would be observed repeatedly. Notably, there were no overlap in cases between Studies 1 and 3. Therefore the main significant finding observed across all three studies (that sleep predicts PM via depressive symptoms) seems more robust.

**Alternative Methods of Analysis**

There are alternate methodological approaches that could have reduced the number of models used in each study. For example, MPlus allows for multiple predicting variables and multiple outcome variables (Muthén & Muthén, 2015). Had we used this approach; we could have investigated the effect of multiple sleep parameters on both sub-types of PM simultaneously. While this approach would have mitigated the issue of multiple comparisons, it would have answered a different research question. Specifically, the results would show if PM was predicted by only the *unique* effect of each sleep variable, *after* accounting for the other sleep variables. This would be helpful if our interest was in which specific type of sleep is important for PM and would have been especially useful if these specific types of sleep could be targeted in treatment. However, from a clinical perspective, this additional information is of less value. Current clinical interventions to improve sleep do not have this degree of specificity; rather than targeting a specific aspect of poor sleep,

\(^{20}\) With the exception of the post-hoc indirect analyses conducted in Study 1.
they generally aim to improve overall sleep quantity and quality (e.g. cognitive behavioural therapy for insomnia Wagley, Rybarczyk, Nay, Danish, & Lund, 2013). Therefore, we argue that this alternative methodological approach was not necessary for the research questions investigated in this thesis.

**Strengths**

A notable strength of this research is the comprehensive, multimodal approach to sleep measurement. Each of these three approaches added something unique to the research that would not have been available with any one of the approaches alone. Firstly, subjective perceptions of sleep quality are important to consider as they provide information about the participants’ experience of their sleep, and this may have a relationship with cognition independent from actual sleep quality (e.g. Draganich and Erdal 2014). It is also valuable to consider subjective sleep measures as this is the most accessible and practical approach to assessing sleep (both clinically and in research). Objective measures, however, are also critical to explore, as they are more likely to give a true estimate of sleep quality. Actigraphy has the advantage of being very widely used in sleep literature, and is rated more highly than the Zeo in terms of ease of use and comfort (Rocknathan et al., 2017), but is limited by its reliance on physical activity to code sleep/wake cycles (Ancoli-Israel et al., 2003). Conversely, consumer EEG devices such as the Zeo can provide more in-depth details of sleep architecture based on brain activity, but are less commonly used and possibly slightly more intrusive than actigraphy (Rocknathan et al., 2017). Considered together these three approaches have provided a comprehensive assessment of sleep in our participants.
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Another notable strength of this research is the use of a well validated, laboratory tested measure of PM (Raskin, 2009). This approach is a notable improvement on previous research that has relied on habitual PM tasks (e.g. button pressing on actigraphy), which may be limited in terms of validity, influenced by the use of reminders, and does not give information about varied types of PM abilities.

Also strengthening findings are the substantial sample sizes used in each of the studies (ranging from 103-170 after exclusion criteria applied). Given the substantial participant commitment required for sleep observation and comprehensive cognitive assessment, many studies that look at sleep and cognition rely on much smaller sample sizes. Importantly, while there was a small amount of participant overlap between studies, the cases included in studies 1 and 3 were entirely independent of each other. Given that each of the studies yielded very comparable findings, this adds strengths to the likelihood that results are reliable.

Limitations and Opportunities for Future Research

Inferring causation.

All results in this thesis are based on cross-sectional observations. Therefore, while offering important information about the potential presence of sleep and PM relationships, findings in this research cannot be used to infer causation. Is tempting to conclude that poor sleep caused cognitive deficits (where they were observed), but it is equally possible that these relationships are bi-directional (Scullin & Bliwise, 2015a). For example, previous research has found that cognitive training can produce improvements in both self-report and objectively measured sleep parameters in older adults (Haimov & Shatil, 2013).
Similarly, where indirect relationships were observed via depressive symptoms, we cannot infer that the depressive symptoms were a result of poor sleep, or that PM difficulties were a result of sleep or depressive symptoms. In fact, it is possible that those with poorer cognition have poorer sleep as a consequence of being more depressed, or that more depression equated to poorer sleep and poorer cognition separately. Future studies could address these alternatives by investigating the relationship between sleep and PM with longitudinal research. Given that data collected in this study were part of a longitudinal research project (HARP), it is even possible that a subset of these same participants may be assessed again in the future. Using the current data as a baseline, future investigations could see if sleep quality predicts PM performance at follow up (in data collected in future years, using the same measures as in the present study). If these participants’ sleep remains stable, but depressive symptoms increase and/or PM abilities decline, this would help support the hypothesis that there may be a directional relationship i.e. poor sleep is resulting in increased depressive symptoms and/or PM decline over time.

**Other paradigms of PM assessment.**

This study used a well validated and practical measure of PM. Our results indicated that, overall, participants did well on this measure, both for the event- and time-based subscales (see Table 1.1 in the General Introduction, Chapter 1). Importantly, however, multiprocess theory suggests several ways that PM task difficulty can be manipulated, which could be investigated in future research (Einstein et al., 2005). For example, PM tasks could assess performance on semantically related cue-action pairs e.g. ‘when I show you a picture of a foot, stamp your feet’, vs on semantically unrelated pairs e.g. ‘when I show you a picture of a lollypop, clap your hands’. Both older and younger adults have been found to have better
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PM performance for related intentions compared with unrelated intentions (Pereira, Ellis, & Freeman, 2012). Moreover, a measure longer than the MIST (with more than 8 items), could investigate different combinations of tasks to further distinguish between more and less demanding PM e.g. related, event-based tasks vs. unrelated, time-based tasks. This distinction may create more variability in performance and be more sensitive to sleep related deficits. Moreover, the time-based/event-based distinction specifically manipulates the executive demand of the task (time-based tasks take more executive control to monitor the environment). However, it is also possible to manipulate the retrospective component of PM e.g. comparing PM success when the participant has more vs fewer tasks to remember at the same time (Meier & Zimmermann, 2015). Given that in our sample, sleep predicted RM more than it did EF in our studies, it could be that making PM tasks more demanding of RM resources may result in a significant effect. Therefore, future research could use a similar design to the current research but investigate performance on these PM subtypes.

Future studies could also build on these findings by considering performance on the PM ongoing task/s. To assess this, experimental PM paradigms could measure performance (e.g. reaction times) on an ongoing task completed on its own vs. while remembering a PM intention. This would indicate how the participant has allocated resources to each task. This is important, because motivated participants may allocate more attention to the PM task at a cost to the ongoing tasks, and so their performance may appear similar even if their overall abilities are compromised (Marsh, Hicks, & Cook, 2005). While there is an ongoing task in 21 While it would have been possible to consider combinations with the MIST, i.e. short–delay, event-based vs long-delay, time-based using, there would have been only 2 items on each subscale (max 4 points) and would unlikely have been sensitive enough to detect sleep-related deficits.
the MIST (the word search), the test does not give a score of performance on this task and
so this hypothesis could not be investigated in the present study.

Of note, since beginning this thesis, Fine et al. (2018) tested an overlapping sample of
HARP participants on PM performance using an experimental PM paradigm (Einstein &
McDaniel, 1990). The study found that longer awakenings, measured with actigraphy,
predicted poorer PM abilities on this task. It also demonstrated that this measure of sleep
disruption in fact mediated the relationship between age and PM performance. Consistent
with the findings presented in the present thesis, this study did not observe any significant
relationships between PM and sleep efficiency or wake after sleep onset, possibly
suggesting that it is the specific features of individual wake episodes that are important for
PM (rather than overall sleep/wake patterns). The candidate was a co-author on this
published paper.

Other measures of sleep.

There are many aspects of sleep that were not investigated in this thesis. The present
study investigated the majority of sleep continuity and architecture variables as
recommended by Ohayon et al. (2017). However, exceptions to this was the investigation
of awakenings of more than five minutes, which was not a variable produced by any of the
sleep measures we used. Importantly, the number of interruptions to sleep may have a
unique effect on cognition in comparison to other measures of interruptions to sleep wake
patterns (e.g. WASO, which is an index of total minutes awake after sleep onset). Future
studies could investigate this by using methods of sleep assessment that provide an estimate
of this variable. If this is not available, another option may be to calculate the average
number of awakenings using the total time spent in WASO, this may give an estimate of
how long the participant was waking for each time. Future studies could also investigate if there is an importance of the specific point in the sleep cycles that arousals occur: for example, awakenings that are coded during SWS may be more problematic than those that occur during light sleep.

Another type of sleep quality that was under-investigated in this study was long sleep. In general, we interpreted our findings of TST with the assumption that more sleep is better. However, we also acknowledged that too much sleep is also emerging in the literature as being problematic for cognitive abilities, possibly just as much as not enough sleep (Scullin & Bliwise, 2015b). Because only very few of our participants met the cut off for too much sleep (just 1-2 in each sample), based on age-group recommendations by Hirshkowitz et al. (2015), we could not investigate this in the present research. However, it may have been that if we had a sample with more long sleepers, we may have observed a negative effect of long sleep on PM abilities, this is something that could be investigated in future studies, e.g. by comparing PM abilities in long vs healthy vs short sleepers to see if there is a difference in performance.

Alternatively, future studies could consider more in-depth features of sleep architecture. While Study 3 in this thesis looked at time spent in specific sleep stages, there may also be specific features of each stage that are important. For example, spindle density in NREM sleep (the mean number of spindles per 30 sec epoch of sleep) may be important for memory consolidation (Gaillard & Blois, 1981; Gaïs, Mölle, Helms, & Born, 2002; Schabus et al., 2004). Future research could investigate if this is also associated with PM performance, either for consolidation of a PM intention or in the context of habitual sleep.
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Of note, all sleep parameters in this thesis were considered as an average across all nights. This approach does not account for intra-individual (night-to-night) variations in sleeping patterns, which may be more sensitive to early sleep changes. Very few previous studies have investigated the possible relationships between sleep variation, and none have looked at PM (for review, see Bei, Wiley, Trinder, & Manber, 2016). This could be an interesting avenue for future research in the context of PM.

Finally, this thesis has not considered the potential influence of daytime naps. This is important, because increased sleep during the day may improve some areas of cognition in both healthy and clinical samples (e.g. Backhaus & Junghanns, 2006; Seeck-Hirschner et al., 2010). It could be that naps serve to compensate for poor sleep quality, which would be consistent with research that states that the majority of naps are compensatory in nature (Ficca, Axelsson, Mollicone, Muto, & Vitiello, 2010). Alternatively, daytime naps may indicate ongoing difficulties with sleep/sleepiness, and therefore result in poorer cognitive performance. In a recent cross sectional study of community-dwelling older adults, Owusu et al. (2019) found that unintentional nappers had poorer immediate word recall than non-nappers, and long-nappers performed more poorly than short-nappers. They also tested participants on EF but did not observe a relationship with daytime naps. Importantly, this study did not investigate PM performance, which could be included in future similar studies. Moreover, this study assessed naps with self-report, and the authors concluded that research with objective measures of naps is needed. Future studies could cross-sectionally or longitudinally investigate if there is an association between naps (number and/or length) and cognitive performance, including PM. For an objective measure, research could consider using actigraphy, which is highly sensitive, although not specific measure for
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daytime naps (Kanady, Drummond, & Mednick, 2011). The Zeo would not be appropriate for this because it can only identify one rest-period per 24 hours, however, this could be something that could be examined in the future if portable means of EGG nap monitoring become available.

**Clinical Implications of Findings**

As outlined in the General Introduction, both sleep and PM have significant consequences for older adults’ well-being and quality of life. PM abilities may even influence how long older adults can stay in independent living. Research in this area is crucial because, as in other countries, the population in Australia continues to age. It is important that we consider how to best support an ageing population to not just live longer, but to keep independence, physical health and psychological health for longer (Andreas et al., 2017; Steptoe, Deaton, & Stone, 2015). The effective assessment, treatment and clinical management of older adults will be an important part of working towards this goal.

The research presented in this thesis has implications for clinical work with older adults. Our preliminary findings suggest that sleep, depressive symptoms and PM difficulties may be related, and could come together in clinical settings. Therefore, it is logical that clinicians working with older adults consider these factors together. For example, a neuropsychologist working with a client complaining of poor PM, could hold in mind that they may also be experiencing sleep and/or depressive symptoms. It may be that part of their recommendations for that client is to refer them for psychological support or sleep intervention.

Likewise, mental health clinicians working with older adults could hold in mind the potential role of sleep and cognition, including PM, in their formulations. We know that up
to one in four older adults experience a mental illness at any one time, and that mood disorders including depression are among the most prevalent mental health conditions in ageing (Andreas et al., 2017). Rather than assessing and treating depression in isolation, our findings suggest that it could also be important to assess for sleep and PM difficulties. Specific assessment around these factors could reveal that a depressed older client may also be struggling with sleep and/or with successfully completing planned tasks, both of which could be contributing to their presentation. Therefore, it is recommended that clinicians routinely assess for difficulties in these areas.

There are various potential approaches to sleep assessment in a clinical context. The findings of this study were similar regardless of measurement approach, suggesting that it is appropriate to start with subjective sleep assessment (e.g. with a self-report diary or questionnaire such as the PSQI). While there are acknowledged limitations to this approach, subjective measures are time and cost effective, non-intrusive and widely accessible. Moreover, as this thesis has shown, self-reported sleep may be associated with depressive symptoms and PM abilities, which have implications for functional outcomes. If responses on self-report measures indicate likely sleep problems in a patient or client, or they are unable to self-report on their sleep (e.g. due to cognitive capacity), further follow up may be required with a referral for a more intensive sleep investigation, possibly including overnight PSG.

Depending on findings from these clinical investigations, part of the treatment plan may be to improve sleep, either by building understanding of sleep hygiene, or by implementing a more thorough, formalised sleep treatment e.g. cognitive behavioural therapy for insomnia (CBT-I; Wagley et al., 2013). It could even be helpful to refer on for a sleep study
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(e.g. if sleep-disordered breathing seems likely). Similarly, if assessment suggests that a client is noticing declines in their PM abilities, it may be helpful to consider neuropsychological assessment. Positively, where PM deficits are a concern, there is growing support for the efficacy of PM interventions. For example, a recent study by Ihle, Albiński, Gurynowicz, and Kliegel (2018), showed that rehearsal training (helping participants practice the maintenance of the PM intention in the intention-retention phase), over four weeks of intervention, was effective in enhancing PM accuracy. This shows that identifying PM deficits in mental health clients may provide increased opportunities for intervention therefore improving our clinical care.

Future research can build on our findings and further inform clinical practice. For example, research could investigate the relationship between sleep and PM in clinical populations, i.e. does the relationship between sleep and PM vary between depressed vs non-depressed participants? To assess this, researchers could identify depression (using either a subjective measure, such as the PHQ-9, or clinical interview), and compare their sleep and PM with healthy controls. If results showed that it is specifically depressed individuals for whom sleep and PM are related, this would further inform highlight the need to assess sleep and PM when working with depressed patients.

Positively, these findings give us some suggestions for possible research which could inform our approaches to clinical intervention. Suggested above are several options for the treatment of PM, depression, or sleep individually. However, given that these factors are related, it may be that improving one of these things has positive implications for the others. There is already evidence that treatments used to improve sleep, like CBT-I, can indirectly improve psychological comorbidities including depression (M. T. Smith, Huang,
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& Manber, 2005). Similarly, CBT-I may have small to moderate benefits for subjectively rated daytime general cognitive functioning (see Herbert, Kyle, & Pratt, 2018 for review). However, review of the literature suggests that no previous studies have investigated the effect of CBT-I on PM performance specifically. Future studies could address this by investigating potential outcomes of sleep interventions on PM, either on its own or via depressive symptoms. For example, participants could have their sleep, depressive symptoms and PM abilities measured at baseline either subjectively (i.e. with the PSQI, PHQ-9 and PRMQ) or, preferably, objectively (with clinical interviews, lab-based cognitive testing and actigraphy or even EEG). Then, participants could participate in CBT-I and have these variables assessed again after the 4 weeks of treatment. If results indicated that these variables improved at follow up, we would have further evidence to suggest that improving sleep has the potential to reduce symptoms of depression and/or improve PM performance. A study of this nature would also potentially offer more support for a causal relationship between sleep and PM, i.e., if PM were to improve with sleep intervention, we could infer that sleep improvement caused PM improvement.

Alternatively, given the bi-directional relationship between cognition and sleep, it may be that targeting PM could also improve sleep. This could be assessed with a similar study design to that outlined above (assessing sleep, depressive symptoms and PM at baseline and then again at follow up) but using a PM intervention (e.g. rehearsal intervention outlined by Ihle et al., 2018). A study such as this could yield crucial findings, because it would support the idea that clinical intervention for PM could help combat the growing cost of poor sleep in Australia. Currently, there is insufficient evidence supporting the crossover of
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treatment approaches, and future studies like these could be instrumental in informing and streamlining the efficacy of our clinical work with older adults.

Summary

The research presented in this thesis is novel in its thorough and detailed approach to investigating the potential relationship between sleep and PM in older adults. The results suggest that while an overall relationship may not exist between sleep and PM, an important indirect relationship may exist between multiple measures of sleep and PM, via the presence of depressive symptoms. Encouragingly, we investigated this in multiple ways, with unique participant samples, and yielded similar results each time. Bearing in mind that data were cross-sectional, not longitudinal, these findings provide tentative evidence that taken together, sleep and depressive symptoms may partially explain variations in PM abilities in older adults. This is an exciting conclusion, as both sleep and depression are potential areas of intervention and treatment, and this may offer avenues for helping older adults improve their PM, an important cognitive domain essential for everyday living.
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